THE LANCET

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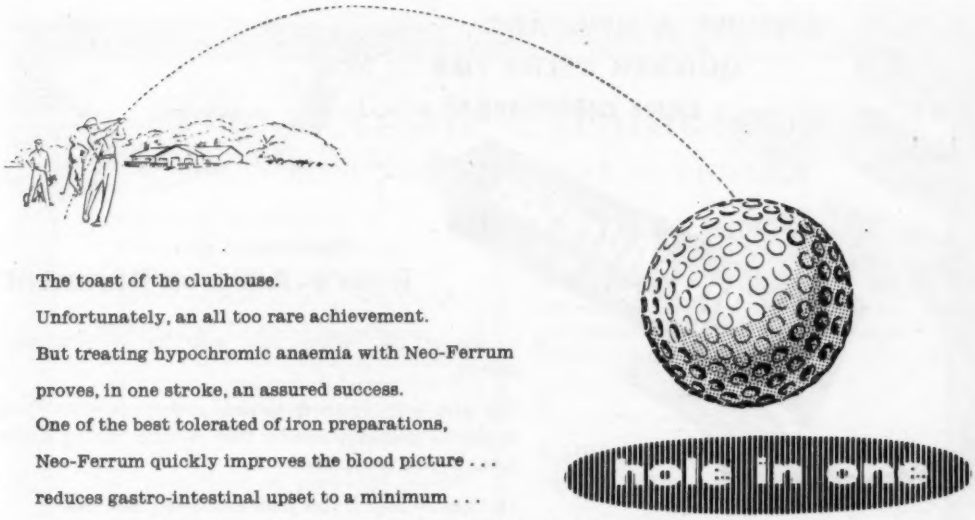

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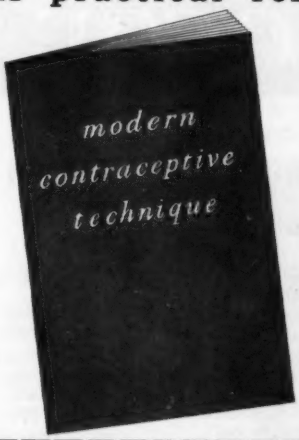

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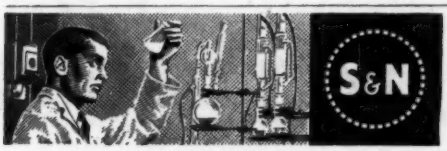
PARAMISAN	**PYCAZIDE**
(*Sodium aminosalicylate B.P.*)	(*Isoniazid B.P.*)
'*Pashets*' 1.5G.	Tablets: 50 mg. 100 mg.
Tablets: 0.5G.	Ampoules: 50 mg. in 2 ml.
Powder (*bulk for dispensing*)	Syrup: 20 and 80 fl. ozs.

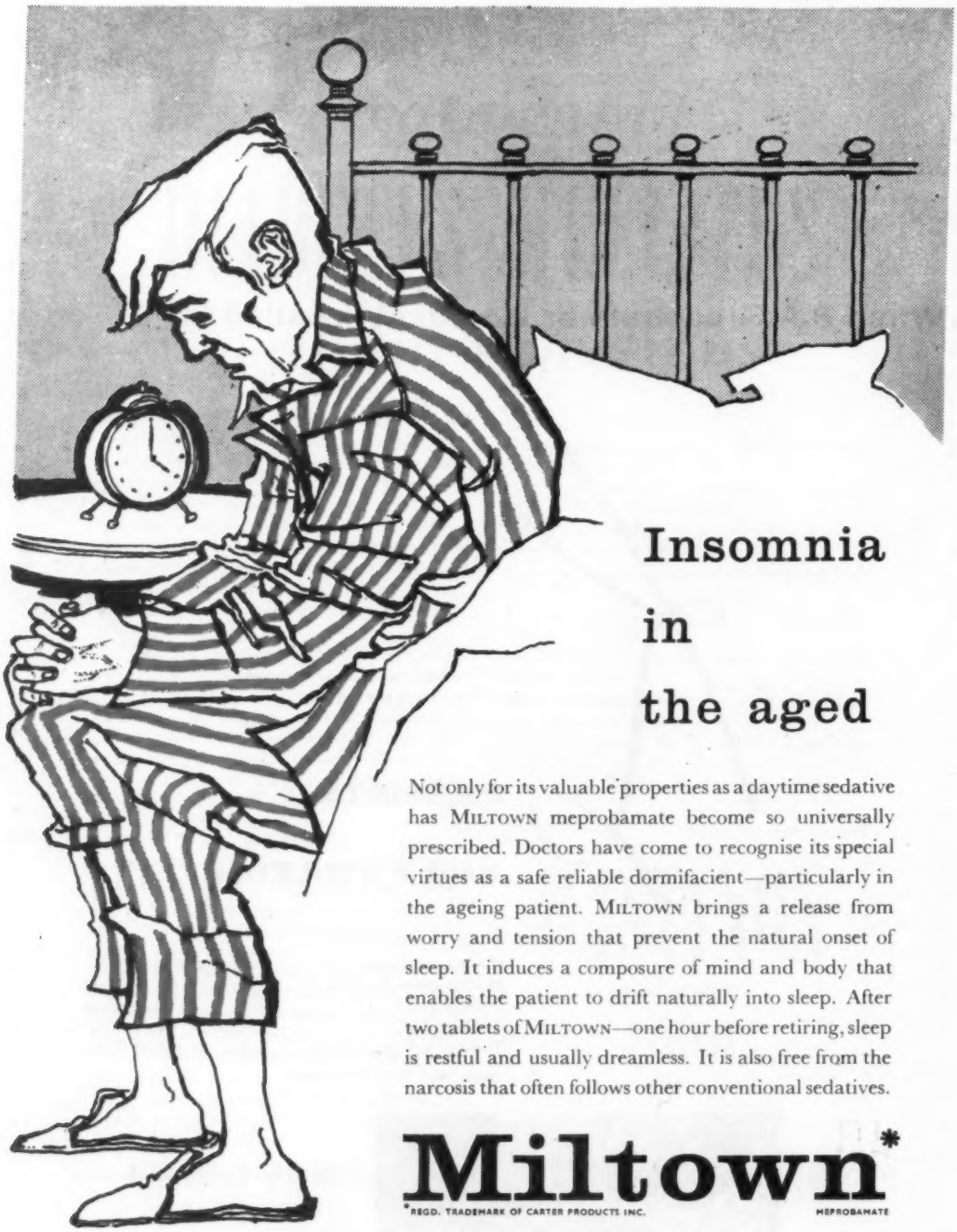
Available at Drug Tariff prices.



'Specialists in tuberculostatic drugs'

SMITH & NEPHEW
PHARMACEUTICALS LTD.

WELWYN GARDEN CITY · HERTS.



Insomnia in the aged

Not only for its valuable properties as a daytime sedative has MILTOWN meprobamate become so universally prescribed. Doctors have come to recognise its special virtues as a safe reliable dormifacient—particularly in the ageing patient. MILTOWN brings a release from worry and tension that prevent the natural onset of sleep. It induces a composure of mind and body that enables the patient to drift naturally into sleep. After two tablets of MILTOWN—one hour before retiring, sleep is restful and usually dreamless. It is also free from the narcosis that often follows other conventional sedatives.

Miltown*

*REGD. TRADEMARK OF CARTER PRODUCTS INC. MEPROBAMATE

Oral tablets of 400 mg. Bottles of 50 and 500

Lederle

LEDERLE LABORATORIES DIVISION

Cyanamid OF GREAT BRITAIN LTD., London, W.C.2

A new molecular complex of

chloral hydrate in tablet form

WELLDORM (dichloralphenazone) tablets are a new molecular compound of chloral hydrate and the analgesic, phenazone. The former problems of taste, odour and gastric upset associated with chloral hydrate have now been overcome by the advent of WELLDORM. Prompt, safe and smooth, non-barbiturate WELLDORM tablets are ideal for those whose primary trouble is just getting to sleep. WELLDORM tablets initiate, then merge with natural physiological sleep. There now opens up a vast new scope for the use of chloral hydrate—long considered one of the best hypnotics therapeutically. Chloral hydrate, as contained in WELLDORM, is one of the safest of all sedatives. In therapeutic doses none of the vital functions is affected. Extensive clinical investigation has revealed no gastric side-effects when WELLDORM has been administered. Clinical samples and literature will gladly be sent on request.

AVAILABILITY: *10 gr. scored tablets in containers of 25 and 250. Prescribable on Form E.C.10.*

Welldorm TABLETS

FOR SAFE SLEEP

S&N SMITH & NEPHEW PHARMACEUTICALS LTD.
WELWYN GARDEN CITY, HERTS.

For the patient who just doesn't get well

PROMOTING

—a return of appetite

—an increase in weight

—a sense of well-being

with Anabolex, the protein-anabolizing, non-virilizing steroid

PATIENTS who are run down or who are recovering from illness frequently suffer from faulty protein metabolism. They are in negative nitrogen balance. Protein, in effect, is being broken down and lost faster than it is being built up.

Anabolex (androstanolone) restores the physiological balance. Many clinical trials have shown that, following the administration of Anabolex, there is an immediate return of the body's capacity to build up protein. The patient feels better, eats better and gains weight.

Here, then, is a physiological "tonic" with a wide therapeutic range. The weakness, lassitude, lack of energy and interest associated with many pathological states may be rapidly overcome by the administration of Anabolex.

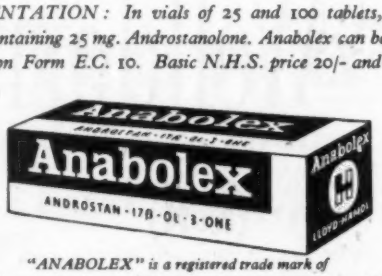
Anabolex can be safely given to patients of all ages and both sexes; in therapeutic doses, its virilizing properties are almost negligible. The only known contra-indication is prostatic carcinoma.

INDICATIONS:

Middle-aged or elderly people who are debilitated or "run down."

Preparation for and recovery from planned surgery. Convalescent patients. Premature infants. The child or adolescent who is under weight. Anorexia. Asthenia. Malnutrition. Wasting diseases.

PRESENTATION: In vials of 25 and 100 tablets, each tablet containing 25 mg. Androstanolone. Anabolex can be prescribed on Form E.C. 10. Basic N.H.S. price 20/- and 70/-.



"ANABOLEX" is a registered trade mark of
Lloyd-Hamol Ltd., 11 Waterloo Place, London, S.W.1

For home massage and relief of local rheumatic pain

Algesal is unique in containing *no counter-irritant*. It is suitable for repeated application by the patient at home, since it will not irritate or redden the skin.

The single, active ingredient is a non-irritating, skin-penetrating salicylate, carried in a soothing white vanishing cream with a pleasant smell of lavender.

INDICATIONS: Fibrositis or muscular rheumatism, osteoarthritis, backache due to lumbo-sacral strain, tenosynovitis, frozen shoulder and local tissue pain after injury or exercise.

Algesal balm gives symptomatic relief in osteoarthritis of the knee

Algesal

non-irritating, skin-penetrating anti-rheumatic salicylate balm

10% *Diethylamine Salicylate, in a soothing vanishing cream.*

Samples and full descriptive literature will be sent on request to the manufacturers

E.G.H. LABS

PERU STREET, SALFORD 3, LANCS.

★ Tear-off pads of leaflets describing a rational home treatment and simple exercises for osteoarthritis of the knee are available for handing to patients. Other leaflets dealing with lumbo-sacral strain and frozen shoulder are also available. Further leaflets are in preparation.

. . . and though there are many—perhaps too many—analgesics available to the practitioner, the balanced properties of Hypon make it a tablet far more effective than most. Extensive tests show that Hypon has the power not only to relieve pain but to do so very rapidly. Constipation, so often encountered following the administration of codeine is effectively counteracted by the addition of phenolphthalein. Caffeine offsets the depressing effects of aspirin and phenacetin. Hypon is invaluable where prolonged administration is called for (chronic rheumatic conditions for instance). Furthermore, the antipyretic properties of Hypon tablets are of particular value in the treatment of the febrile states of influenza, tonsillitis . . .

HYPON

rapidly relieves pain

Acid Acetylsalicyl. B.P.	40.22%	Codein. Phosph. B.P.	0.99%
Phenacet. B.P.	48.00%	Phenolphthal. B.P.	1.04%
Caffein. B.P.	2.00%	Excip.	7.75%

(Each tablet 5 grains)

CALMIC LIMITED · Crewe: *Crewe 3251-5* London: *2 Mansfield Street · W1 · Langham 8038-9*

Nasal Congestion?

Neither ephedrine nor adrenaline give such sustained relief as Neophryn . . . yet Neophryn is safer than either. Neophryn produces effective decongestion without unpleasant side effects such as C.N.S. stimulation, sedation, or secondary congestion. It is safe for infants and children as well as adults, and is widely prescribed for the common cold, sinusitis and allergic rhinitis. Neophryn is also available with antihistamine.

Medical literature is available on request

Neophryn gives relief without secondary congestion

Trade Mark

Neophryn is a sympathomimetic amine (1-m-hydroxy-α-methylaminomethyl benzyl alcohol HCl) in aqueous solution; available as a spray or drops

Basic N.H.S. cost of Nasal Spray or Drops 2/4. With antihistamine (in spray form only): 2/8

Bayer Products Limited
Neville House, Kingston-on-Thames, Surrey.
Associated exporting company: Winthrop Products Limited

BAYER

15

A new approach to the treatment of Rheumatoid Disease

RECENT WORK has shown that chloroquine administered in small daily doses (1-2 tablets 'Avloclor') can produce good to excellent results in the control of rheumatoid disease, particularly rheumatoid arthritis. The treatment is safe and free from serious side-effects. Moreover, unlike the steroids, it has the advantage that it can be given over a prolonged period without influencing the adrenal, the pituitary, or any other internal function.

'Avloclor' *Chloroquine Phosphate B.P.*

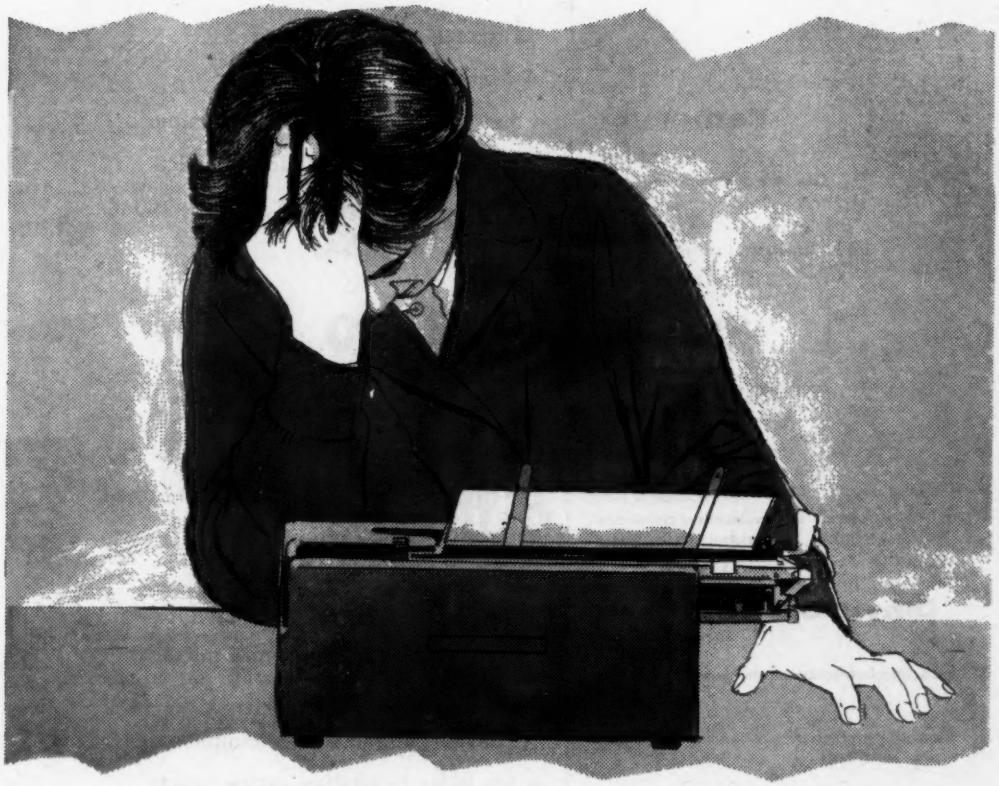
Issued in bisected tablets of 0.25 gramme
(equivalent to 0.15 gramme base)

Literature and further information available on request

IMPERIAL CHEMICAL INDUSTRIES LIMITED Pharmaceuticals Division Wilmslow Cheshire

Ph.791

a specific treatment for spasmodic dysmenorrhœa . . .



The disadvantages of analgesics in the treatment of spasmodic dysmenorrhœa are familiar. Constipation, gastric upsets and diminished alertness are well known side-effects.

A distinct step forward has been achieved by the introduction of Buscopan, an anti-spasmodic which, by relieving spasm of the uterine muscle, represents a remedy that effectively alleviates the condition. Buscopan relieves uterine spasm safely and swiftly and is not just a symptomatic treatment.

Buscopan is virtually free from side-effects and has no adverse effect on the central nervous system—this makes it additionally acceptable in the treatment of spasmodic dysmenorrhœa.

BUSCOPAN*

Hyoscine-N-Butylbromide

Manufactured and distributed in the U.K. by Pfizer Ltd., Folkestone, Kent, for

C. H. Boehringer Sohn, Ingelheim-am-Rhein.

Registered Proprietors of the Trade Mark. **Regd. Trade Mark.*

124300

In the treatment of migraine . . .

* **Femergin**

TABLETS
1 mg. Ergotamine Tartrate B.P.

AMPOULES
0.5 mg. Ergotamine Tartrate B.P./ml.

Cafergot

TABLETS
1 mg. Ergotamine Tartrate B.P.
100 mg. Caffeine B.P.

SUPPOSITORIES
2 mg. Ergotamine Tartrate B.P.
100 mg. Caffeine B.P.
0.25 mg. total alkaloids of belladonna
100 mg. isobutylallyl barbituric acid

Dihydroergotamine

SOLUTION
2 mg. dihydroergotamine methanesulphonate/ml.

AMPOULES
1 mg. dihydroergotamine methanesulphonate/ml.

"If ergotamine tartrate
by itself is not effective,
it may be more effective when combined
with caffeine, such as Cafergot tablets
(ergotamine tartrate 1 mg., caffeine 100 mg.)
or rectal suppositories . . .

If Cafergot tablets
and rectal suppositories are used
the initial dose should not exceed
2 tablets or 1 suppository,
and the total daily dose should not exceed
6 tablets or 2 suppositories.

Some patients develop nausea
and vomiting with ergotamine tartrate,
and the newer preparation
dihydroergotamine methanesulphonate (D.H.E.45)
is less liable to produce gastric upsets
but is not so generally effective . . ."

British Encyclopaedia of Medical Practice,
Interim Supplement No. 181 — October 1957, page 12

ALL BY **SANDOZ**

* The original Ergotamine Tartrate B.P.
(marketed outside the British Isles as Gynergen)

Sandoz Products Limited

Sandoz House
23 Great Castle Street
London, W.1

Senokot is cheaper by half than paraffin

FROM THE BRITISH MEDICAL JOURNAL, AUGUST 11, 1956, p.374.

"In these days of economy in prescribing . . .
the biologically standardized form of senna [Senokot]
. . . is cheaper by half than paraffin."

	BASIC N.H.S. PRICES (*Tax free D.P.s*)	RETAIL PRICES (*Including Tax*)
SENOKOT GRANULES:	2lb, 21/-	2oz, 2/10; 6oz, 7/9
SENOKOT TABLETS:	1,000, 16/-	50, 2/5; 200, 7/3

On E.C.10: Cost about a halfpenny a dose

WESTMINSTER LABORATORIES LTD., CHALCOT ROAD, LONDON, N.W.1

G1398

Almost the worst thing about 'flu is getting over it

To the mentally depressed and bodily fatigued post-influenzal patient, METATONE* brings a quick return to normal vigour. Combining appetite-promoting vitamin B with mineral glycerophosphates and strychnine, Metatone has an outstanding capacity for speedily restoring normal metabolic function.

METATONE

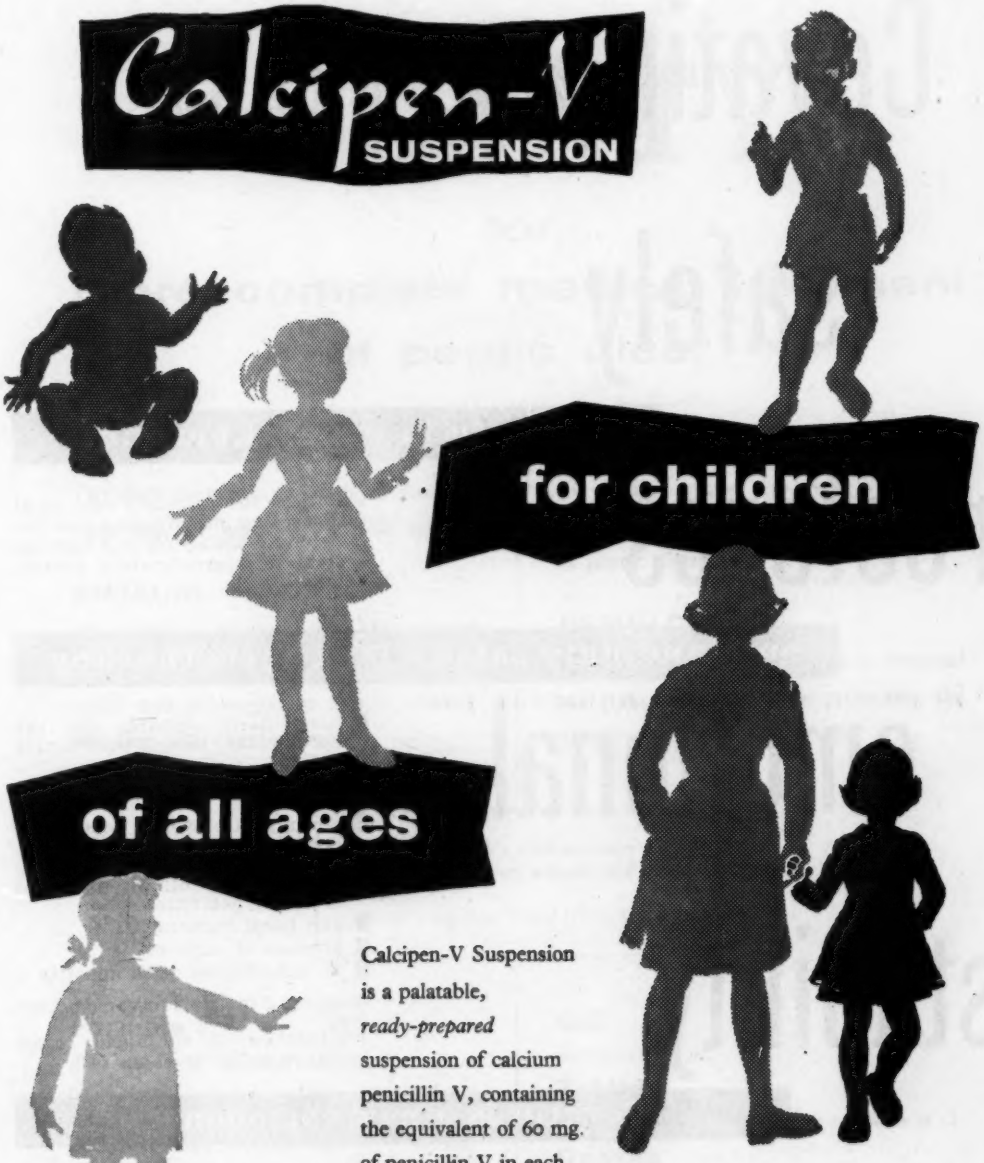
** Trade Mark*

speeds recovery

PARKE, DAVIS & COMPANY LTD. (Inc. U.S.A.) HOUNSLOW · MIDDLESEX · Telephone: Hounslow 2361
AND AT CARFIN INDUSTRIAL ESTATE, CARFIN, LANARKSHIRE. HOLYTOWN 326/7

164

Calcipen-V SUSPENSION



for children

of all ages

Calcipen-V Suspension is a palatable, *ready-prepared* suspension of calcium penicillin V, containing the equivalent of 60 mg. of penicillin V in each 5 ml. It is supplied in bottles of 60 ml. Calcipen-V is also supplied as tablets containing the equivalent of 60, 125 or 250 mg. of penicillin V. Professional sample and detailed literature gladly sent on request.

BOOTS PURE DRUG CO. LTD., NOTTINGHAM, ENGLAND

Boots

Covatin safely restores emotional stability

Covatin in general practice

stabilises the patient's emotional responses by maintaining the two divisions of the autonomic nervous system in approximately normal balance.

outstandingly safe in long-term therapy

- particularly suitable for the chronically tense, over-active patient
- low toxicity and freedom from side effects
- non hypnotic, even at high dosage levels
- alertness is unimpaired, so the patient can follow his usual everyday activities
- non habit forming
- absence of euphoria
- no interference with appetite

Dosage: 1-2 tablets, 3 times a day with food.
Presentation: 50 mg. sugar coated tablets in bottles of 50 and 500.

Covatin is a new compound

With entirely new chemical and pharmacological properties for the specific treatment of emotional instability.

Covatin
TRADE MARK

WILLIAM R. WARNER & CO. LTD., EASTLEIGH, HAMPSHIRE.

COV 587/4

1.556

KOLANTYL

for more complete medical treatment of peptic ulcer

ANTISPASMODIC

To reduce ulcer pain and to delay stomach emptying, so assisting antacid action.

ANTACID

To neutralise excess acid. The antacid component of 'Kolantyl' is virtually ideal; rapid and prolonged in action, neither laxating nor constipating.

ANTILYSOZYME

To inhibit excess lysozyme, which is believed to be a factor in the aetiology of peptic ulcer.

DEMULCENT

To ensure ingredients adhere to mucosal surfaces and to assist in protecting the ulcer crater.

"... may be safely tried out under G.P. conditions with every prospect of a good result ..."
Medical World (1955) 82: 379

Formula

Each tablet or 10 c.c. of Gel contains:

'Merbentyl' (diethylaminocarbethoxybicyclohexyl hydrochloride)	5 mg.
Dried Aluminium Hydroxide Gel	400 mg.
Heavy Magnesium Oxide	200 mg.
Sodium Lauryl Sulphate	25 mg.
Methylcellulose	100 mg.

Gel

Bottles of 12 fl. oz.

Tablets

Cartons of 48 and 240 tablets in roll packs of 12.

Dosage

1 to 2 tablets (2 to 4 teaspoonfuls of Gel) 3 or 4 times a day.

Merrell Research

'Kolantyl' and 'Merbentyl' are registered trade marks of the Wm. S. Merrell Co.

Distributed in Great Britain and Republic of Ireland by
RIKER LABORATORIES LTD.
LOUGHBOROUGH, LEICS.

RHINITIS

— Rapid *SOOTHING* effect

— Prolonged *DECONGESTANT* effect

Cortibiotic

ROUSSEL

nasal drops

The irritation which often accompanies rhinitis is soon relieved by the local anti-inflammatory effect of the corticosteroid, prednisolone acetate (0.25%).

The congestion is rapidly controlled with a vaso-constrictor, phenylephrine (0.25%), and this effect is prolonged by the lasting anti-inflammatory action of prednisolone.

The local antibiotic, Soframycin (1.25%), is added as a precaution against primary and secondary bacterial invasion.

INDICATIONS

Acute rhinitis
Allergic rhinitis (hay fever and perennial)
Sinusitis

PACKING

Dropper bottle of 8 ml. aqueous isotonic suspension.

ROUSSEL
LONDON N.W.10
LADbroke 6611

"Never neglect the opportunity of learning from another doctor: in this context about the contents of his bag"

Practitioner (1957) 179, 626

Bellergal

BY **SANDOZ**

is in the bag!*

Bellergal is always at hand for the symptomatic treatment of a wide variety of **psychosomatic disorders**

TABLETS: 0.1 mg. total alkaloids of belladonna
0.3 mg. Ergotamine Tartrate B.P.
20 mg. Phenobarbitone B.P.

* Bellergal has a place in "*The Doctor's Bag*"—*Practitioner* (1957) 179, 624

Sandoz Products Limited

Sandoz House
23 Great Castle Street
London, W.1

***L

New

DISTAQUAINE V-K

Potassium penicillin V

a chemically improved form of 'DISTAQUAINE' V

* **greater solubility**
* **faster absorption**
* **earlier peak blood levels**
* **higher therapeutic concentration**

DISTAQUAINE V-K

Each tablet contains the equivalent of 125 mg. penicillin V acid (as potassium salt):

Dosage: One or more tablets, depending upon the severity of the infection, at four-hourly intervals.

DC&B·L

THE DISTILLERS COMPANY (*Biochemicals*) LIMITED

Broadway House, The Broadway, Wimbledon, London S.W.19 Tel: Liberty 6600.

Owners of the trade mark 'DISTAQUAINE'

PPH5/38

ENAVID*

BRAND OF NORETHYNODREL AND ETHYNYLOESTRADIOL 3-METHYL ETHER

For the specific control of menstrual irregularities

ENAVID, containing the new Searle steroid norethynodrel, permits *specific* and usually complete *control* of the menstrual cycle on *oral* administration and thus provides effective therapy for most menstrual irregularities.

ENAVID has strong progestational and a lesser oestrogenic activity on the endometrium, which stimulates its development to a secretory phase. It also inhibits the secretion of gonadotropins by the anterior pituitary gland.

ENAVID is therefore recommended for:

- **AMENORRHOEA** (Primary and Secondary)
- **OLIGOMENORRHOEA**
- **MENORRHAGIA**
- **METRORRHAGIA**
- **DYSMENORRHOEA**
- **PREMENSTRUAL TENSION** and the
- **"INADEQUATE LUTEAL PHASE"**

ENAVID is supplied as 10 mg. tablets in bottles of 20 and 50 tablets.

Detailed literature is available on request.

* *Trade Mark.*

SEARLE

G. D. SEARLE & CO., LTD., HIGH WYCOMBE, BUCKS. Tel. High Wycombe 1770

EN : PI17

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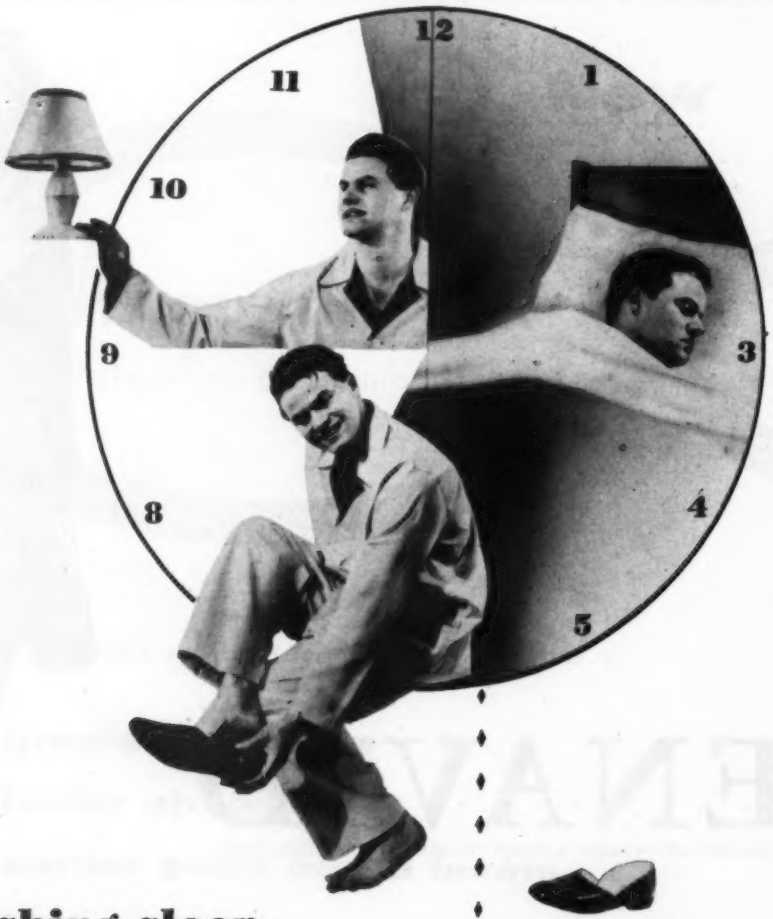


for refreshing sleep and a fresh awakening

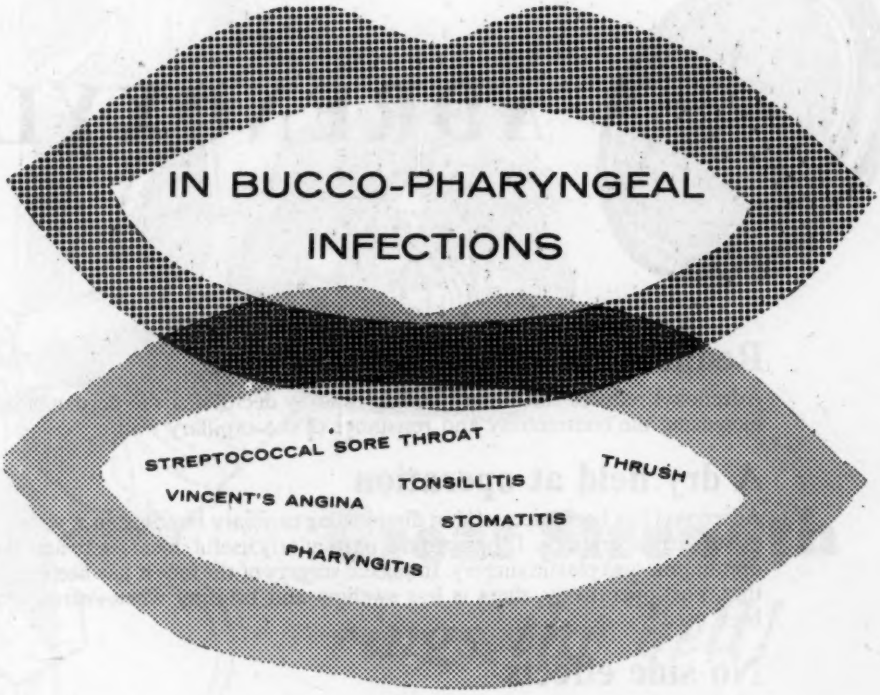
Effective against all types of insomnia not due to pain, CARBRITAL* provides a combination of pentobarbitone sodium, a rapid-acting barbiturate, with carbromal, a mild sedative. This combination ensures the speedy onset of sleep and gently sustains it throughout the night, with little or no depression the following day.

CARBRITAL

*Trade Mark

In bottles of 25 and 250 capsules each containing pentobarbitone sodium (1½ grs.) and carbromal (4 grs.)
Also as Carbrital Elixir.

Parke, Davis & Company, Ltd. *(Inc. U.S.A.)* · Hounslow · Middlesex · Telephone: Hounslow 2361



DEQUADIN

- rapidly and effectively controls the infection
- avoids the risks involved in local antibiotic therapy
- is more widely effective against oral pathogens than penicillin
- is fully active in the presence of serum
- is completely non-toxic

DEQUADIN LOZENGES

Available as DEQUADIN LOZENGES, in tubes of 20 lozenges.

Dosage: One lozenge sucked slowly every 2 or 3 hours.

STANDARD REFERENCE CARD ON APPLICATION

Manufactured in England by ALLEN & HANBURYS LTD LONDON E2

N 58 112 H

ADRENOXYL

Reduces the mean bleeding-time

Adrenoxyl reduces the mean bleeding-time by decreasing the permeability and increasing the contractility and resistance of the capillary wall.

A dry field at operation

Adrenoxyl has been successful in diminishing capillary bleeding in a wide range of surgical operations. It has proved particularly useful in ear, nose and throat, ophthalmic and plastic surgery. In plastic surgery of the face it has been reported that, post-operatively, there is less swelling and bruising when Adrenoxyl has been used.

No side effects

Adrenoxyl does not have any side effects or contraindications. It does not affect blood coagulation, blood pressure or pulse rate and does not possess any sympathomimetic properties.

In medical conditions

Adrenoxyl has been used with success in those medical conditions associated with capillary fragility.

In the British Medical Journal (April 21st, 1956) a correspondent confirmed the value of Adrenoxyl in providing a dry field for the surgeon and in shortening the duration of the operation.

Packs

Ampoules: Boxes of 6 and boxes of 50.
Each ampoule contains 0.75 mg. of adrenochrome monosemicarbazone dihydrate.

Tablets: Tubes of 25 and bottles of 500.
Each tablet contains 2.5 mg. of adrenochrome monosemicarbazone dihydrate.

The best results are obtained when both tablets and ampoules are used.

HORLICKS LIMITED

Pharmaceutical Division Slough Bucks

Literature and samples are available on request to the Medical Information Dept.

Great Strength

rings the bell!

Uniquely strong . . . swift-acting . . . yet amply safe for children . . . 'Actidil' can provide a surer, more decisive answer to the nagging challenge of general allergic symptoms. This modern antihistamine gives relief within minutes. It has little tendency to evoke unwanted side-effects. Its benefits persist for some twelve hours. For adults, 'Actidil' is available as tablets; for children, as a pleasant tangerine-flavoured elixir. Given in either form it holds the promise of new comfort for many, if not all, of your allergic patients . . . today . . . and in the "pollen months" ahead.

TABLETS: (2·5 *mgm.) in bottles of* 25, 100 *and* 500
ELIXIR: (1 *mgm. per fluid drachm) in bottles of* 20 *fl. oz.*

'ACTIDIL'
BRAND
TRIPROLIDINE HYDROCHLORIDE

Today's most potent antihistamine . . .
yet safe for your youngest patient

BURROUGHS WELLCOME & CO., LONDON
(THE WELLCOME FOUNDATION LTD.)

'Marsilid'

TRADE MARK BRAND

IPRONIAZID

'Marsilid' is a potent amine oxidase inhibitor and, as a consequence, intervenes in the metabolism of amines such as serotonin, adrenaline and noradrenaline. It is probable that this property of 'Marsilid' accounts for many of the observed clinical effects of this drug.

The clinical uses of 'Marsilid' include:

DEPRESSIVE STATES

The typical reaction to isoniazid consisted of a feeling of well-being, accompanied by improved appetite, increased energy and diminution of sleep requirements.

J. nerv. ment. Dis., 1956, 124, 322.

ANGINA PECTORIS

In man, the administration of iproniazid resolves the syndrome of angina, relieving pain and increasing the capacity for effort.

Arch. Inst. Cardiol. (Mexico), 1957, 27, 563.

RHEUMATOID ARTHRITIS

The favourable effects of the hydrazides, especially iproniazid, on subjective manifestations in patients with rheumatoid arthritis were the most interesting and perhaps the most significant findings of this study.

Cleveland Clin. Quart., 1957, 24, 90.

Marsilid Tablets 50 mg. in packings of 100.

ROCHE PRODUCTS LIMITED, 15 MANCHESTER SQUARE, LONDON, W.1

EFFECTS OF LINOLENIC AND STEARIC ACIDS ON CHOLESTEROL-INDUCED LIPOID DEPOSITION IN HUMAN AORTIC CELLS IN TISSUE-CULTURE *

DAVID D. RUTSTEIN
M.D.
PROFESSOR OF PREVENTIVE MEDICINE
ESTELLE FASOLINO INGENITO
Ph.D.
RESEARCH ASSOCIATE IN PREVENTIVE MEDICINE
JOHN M. CRAIG
M.D.
ASSISTANT PROFESSOR OF PATHOLOGY AT THE CHILDREN'S HOSPITAL
MARCELLO MARTINELLI †
M.D.
RESEARCH FELLOW IN PREVENTIVE MEDICINE
HARVARD UNIVERSITY MEDICAL SCHOOL, BOSTON, MASSACHUSETTS
With the Technical Assistance of
MARY LOU FOLEY, B.A., *and* BURTON GOLDBERG, B.S.
From the Departments of Preventive Medicine and Pathology, Harvard University Medical School, and the Department of Pathology of The Children's Medical Center, Boston, Massachusetts

A CHANCE observation in our laboratory led to the study of factors affecting lipoid deposition in tissue-cultures of cells from the human aorta. The effects of steroids, such as cortisone, on sodium and potassium exchange between the medium and human heart-cells in tissue-culture were under study. Cholesterol, a steroid without known direct effect on sodium and potassium exchange was added to one of the control cultures. After eight days' growth cells exposed to cholesterol were found to contain granules which stained with sudan IV and with Liebermann-Burchard reagents. This observation led us to initiate studies on the deposition of lipoid in tissue cultures of human aortic lining in a medium containing human blood-serum.

Materials and Methods

Standardised stock tissue-cultures of cells from human aorta are grown by a method originally developed in this laboratory for growing cells from fragments of human heart (Ingenito et al. 1958).

Briefly, sterile resected coarctations of the aorta ‡ are quickly transferred to the laboratory, and their inner lining is stripped off and cut into pieces about 1 mm. in diameter. These fragments are planted in Earle 'T-60' flasks on a plasma clot in a medium containing 40% human blood-serum, 20% chick-embryo extract$_{50}$, and 40% Hanks' balanced salt solution (Scherer et al. 1955). Other constituents of the medium are 0·002% phenol red, penicillin-G 100 units, and streptomycin sulphate 50 μg. per ml. of medium.

In all the experiments, observations are made in duplicate. Two Earle 'T-15' flasks, each containing two transplants of growing aortic tissue from stock cultures in T-60 flasks, are prepared for each control and for each experimental medium. After transfer to the T-15 flasks all the cultures are incubated at 37·5° C for four days, by which time growth is usually luxuriant. At this point the medium is replaced by control medium or by experimental media containing cholesterol, or fatty acid, or both.

Cholesterol is added to the medium in two different ways—in ethanol solution and in aqueous solution bound to beta-lipoprotein.§

The ethanol solution is prepared and added as described for other steroids (Leonard and Rutstein 1953).

Briefly, a freshly prepared solution of cholesterol (*U.S.P.*, Merck) 300 mg. per 100 ml. in 95% ethanol is slowly diluted, with constant stirring, by the addition of Hanks' balanced salt solution to a final concentration of 1 to 15 ethanol-in-salt solution. Aliquots of this solution are incorporated into the medium to final concentrations of 1–5 mg. of cholesterol per 100 ml. The ethanol concentration is maintained constant in all the flasks in each experiment by adding appropriate amounts of a 1 to 15 ethanol-in-salt solution to those

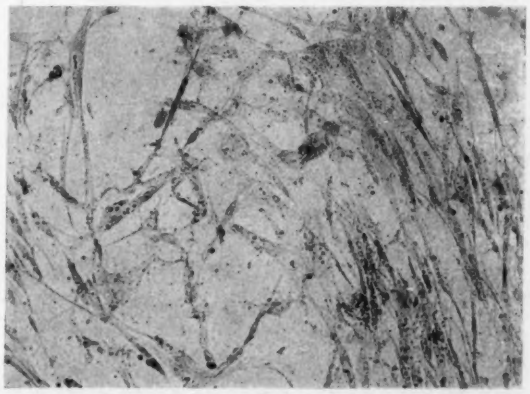


Fig. 1—Control. Human aortic tissue (donor M. B.) after five days in normal medium (serum donor T. G.). Figs. 2-15 concern the same donors. In this and subsequent illustrations (figs. 2-35) the tissue was stained with sudan IV and is magnified ×130.

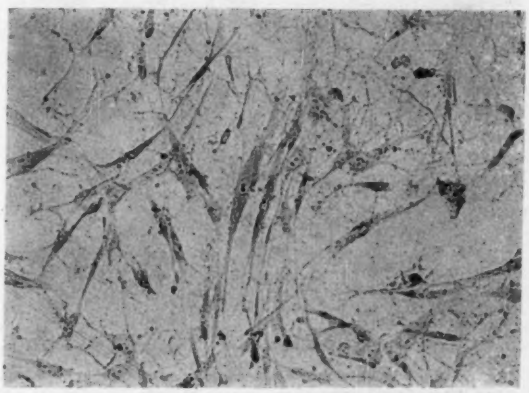


Fig. 2—After five days in normal medium plus 1·5% ethanol.

* This study is supported by a grant from the American Heart Association. We are also indebted to M. and Mme. Pierre Lepaulle of Paris, France, for the Marie Laure Fund for Research in Rheumatic Fever and Related Diseases at the Harvard Medical School. This Fund made possible the original research from which the present study evolved.

† Lederle Research Fellow from the University of Bologna (Prof. Giulio Sotgiu).

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§ We are indebted to Dr. John Lawrence Oncley, professor of biological chemistry, Harvard University Medical School, and his staff for making available to us freshly prepared solutions of cholesterol bound to beta-lipoprotein of density 1·03 (Oncley et al. 1957).

cultures in which the medium contains less than the maximum amount of cholesterol.

Preliminary experiments show that concentrations of ethanol up to 2·5% by volume do not have any visible effect on either cell proliferation or cell morphology. In all the experiments in which cholesterol was added in ethanol, the ethanol concentration never exceeded 1·75%, and in most cases it was not more than 1·4%.

By the second method, cholesterol bound to beta-lipoprotein was added in concentrations of 10–70 mg. of bound cholesterol per 100 ml. Combining the beta-lipoprotein solution and the constituents of the medium in the cold at 4° C always yielded clear solutions.

The fatty acids are added by diluting stock ethanol solutions (linolenic acid 5 g. per 100 ml.; stearic acid 1·25 g. per 100 mls.) with medium. The amount of ethanol added to the medium

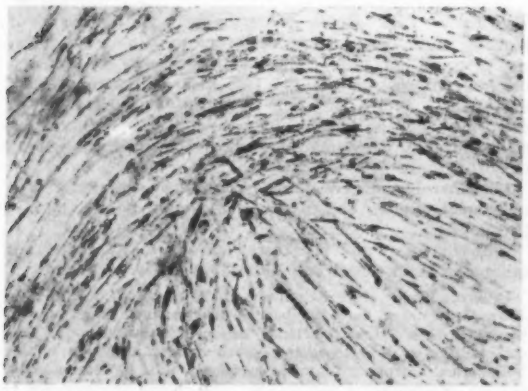

Fig. 3—After five days in normal medium plus cholesterol 1 mg. per 100 ml. in ethanol.

Fig. 6—After five days in normal medium plus cholesterol 5 mg. per 100 ml. in ethanol.

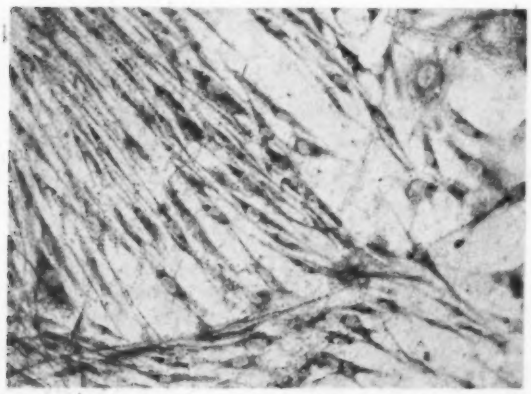

Fig. 4—After five days in normal medium plus cholesterol 2 mg. per 100 ml. in ethanol.

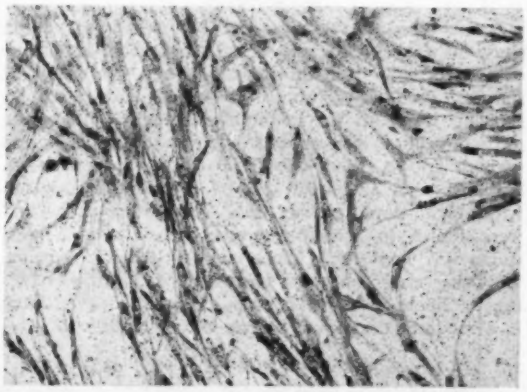

Fig. 7—After five days in normal medium plus cholesterol 3 mg. per 100 ml. in ethanol followed by five days in normal medium.

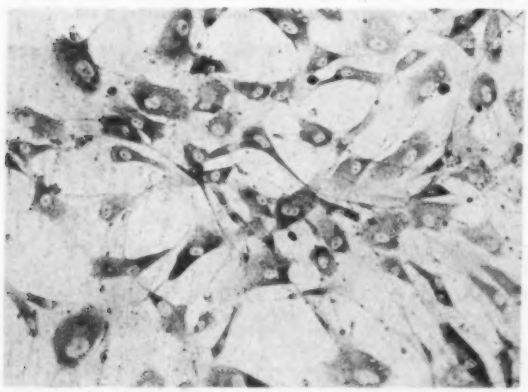

Fig. 5—After five days in normal medium plus cholesterol 3 mg. per 100 ml. in ethanol.

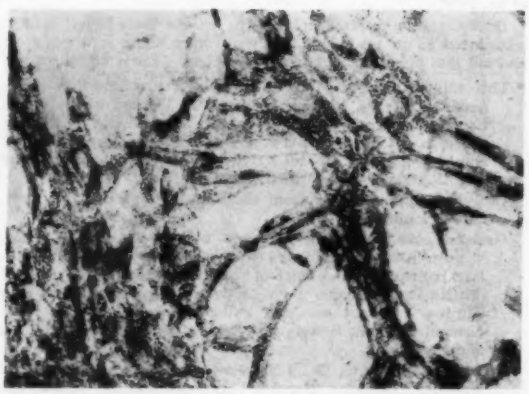

Fig. 8—After five days in normal medium plus cholesterol 3 mg. per 100 ml. in ethanol followed by two more days in the same medium.

containing the highest concentration of fatty acid is negligible—linolenic acid 0·02% and stearic acid 0·08%.

The intracellular deposition of lipoid—usually first noted on the fourth or fifth day and reaching a maximum on the fifth to eighth day after the experiment is begun—is confirmed by staining with sudan IV. In certain experiments, as already stated, the cells are stained with Liebermann-Burchard reagents. In each experiment comparisons are always made with tissue fragments from the same stock culture in normal medium.

In the photographs as reproduced here the magnification is approximately 130.

Results

Deposition of Lipoid in Tissue when Cholesterol is added in Ethanol Solution.

The control culture (fig. 1) and that to which 1·75% ethanol has been added—the ethanol control (fig. 2)—look alike at seven days. Lipoid deposition begins to

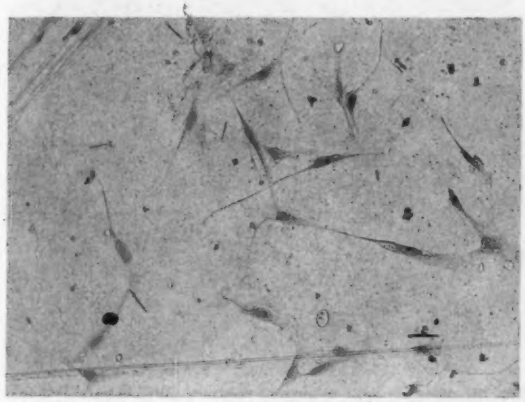

Fig. 9—Control. After six days in normal medium.

Fig. 10—After six days in normal medium plus 1·5% ethanol.

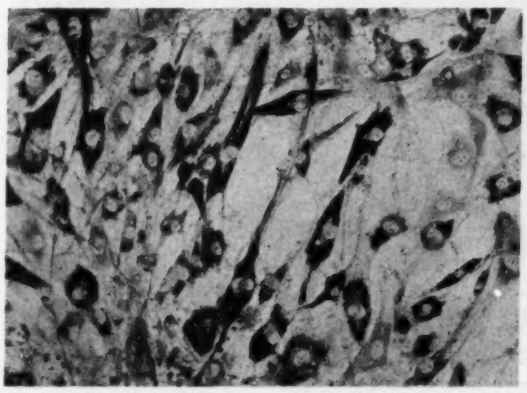

Fig. 11—After six days in normal medium plus cholesterol 3 mg. per 100 ml. in ethanol.

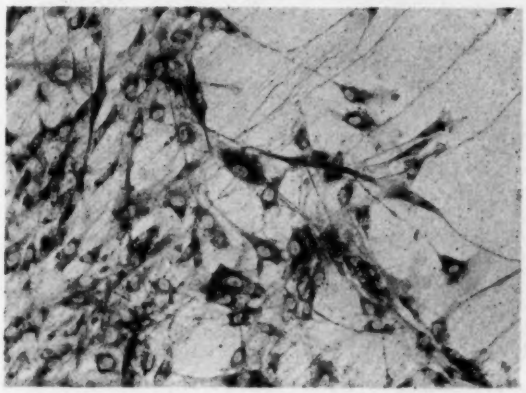

Fig. 12—After six days in normal medium plus cholesterol 3 mg. per 100 ml. in ethanol and linolenic acid 0·005 mg. per 100 ml.

Fig. 13—After six days in normal medium plus cholesterol 3 mg. per 100 ml. in ethanol and linolenic acid 0·05 mg. per 100 ml.

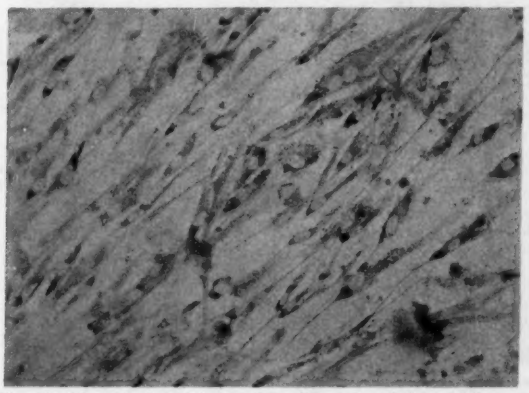

Fig. 14—After six days in normal medium plus cholesterol 3 mg. per 100 ml. in ethanol and linolenic acid 0·5 mg. per 100 ml.

appear when cholesterol has been added at a concentration of 1 mg. per 100 ml. (fig. 3) and is more clearly seen at 2 mg. (fig. 4). At a concentration of 3 mg. of added cholesterol per 100 ml., intracellular deposition of lipoid is clearly seen (fig. 5) and is always associated with enlargement of the entire cell, including the nucleus. These changes are even greater when the concentration of the added cholesterol is 5 mg. per 100 ml. (fig. 6). The intracellular lipoid stains with the Liebermann-Burchard reagents as well as with sudan IV. When polarised light is passed through the lipoid particles, the plane of light is not rotated.

When the medium containing added cholesterol 3 mg. per 100 ml. (fig. 5) is replaced at eight days with

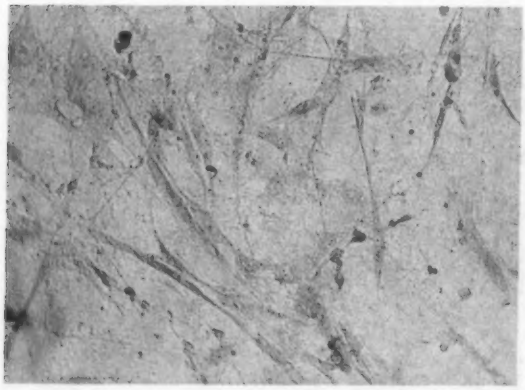

Fig. 15—After six days in normal medium plus cholesterol 3 mg. per 100 ml. in ethanol and linolenic acid 1 mg. per 100 ml.

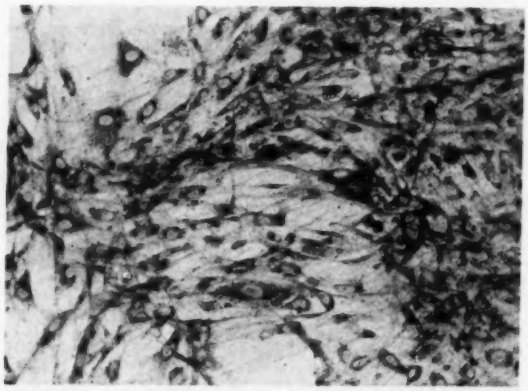

Fig. 18—After six days in normal medium plus cholesterol 3 mg. per 100 ml. in ethanol.

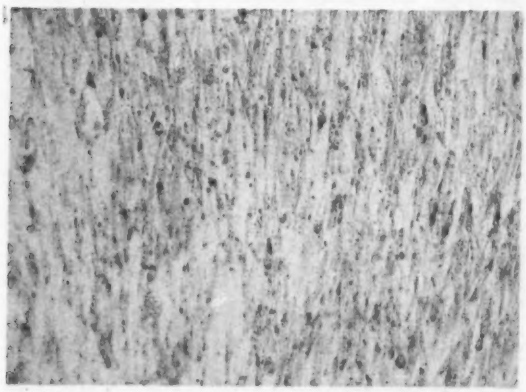

Fig. 16—Control. After six days in normal medium (aortic tissue donor D. L., serum donor T. G.). The same donors apply in figs. 17-22.

Fig. 19—After six days in normal medium plus cholesterol 3 mg. per 100 ml. in ethanol and linolenic acid 1 mg. per 100 ml.

Fig. 17—After six days in normal medium plus 1·5% ethanol.

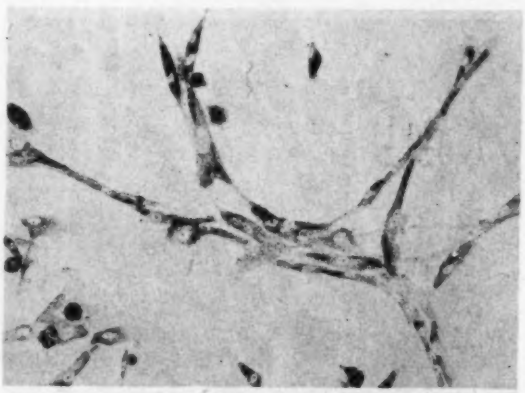

Fig. 20—After six days in normal medium plus cholesterol 3 mg. per 100 ml. in ethanol and stearic acid 1 mg. per 100 ml.

normal medium, the cells gradually regain their normal appearance by the end of five more days (fig. 7), but some deposited lipoid remains. On the other hand, if the cultures are fed again with medium containing the same concentration (3 mg. per 100 ml.) of cholesterol, all the cells show increased deposition of lipoid (fig. 8) and die during the next two days.

Inhibition by Linolenic Acid of Tissue Lipoid Deposition when Cholesterol is added in Ethanol Solution

There are slight differences within the range of normal between the control and the ethanol control cultures (figs. 9 and 10). Cultures to which cholesterol 3 mg. per 100 ml. has been added in ethanol show deposition of lipoid (fig. 11). When increasing amounts of linolenic

Fig. 21—After six days in normal medium plus linolenic acid 1 mg. per 100 ml.

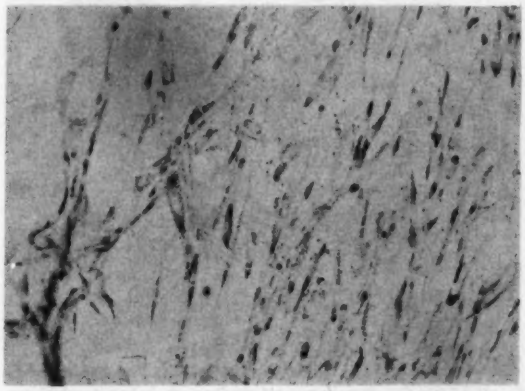

Fig. 22—After six days in normal medium plus stearic acid 1 mg. per 100 ml.

Fig. 23—Control. After five days in normal medium (aortic tissue donor S. B., serum donor A. L.). The same donors apply in figs. 24-27.

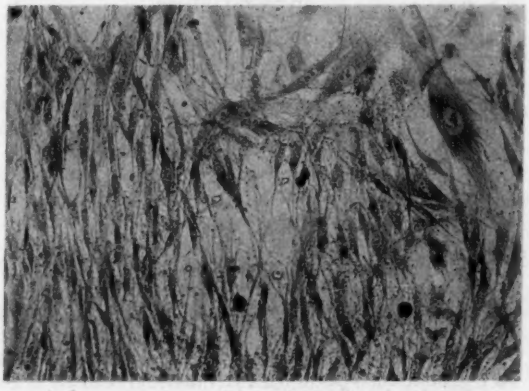

Fig. 24—After five days in normal medium plus cholesterol 10 mg. per 100 ml. in beta-lipoprotein solution.

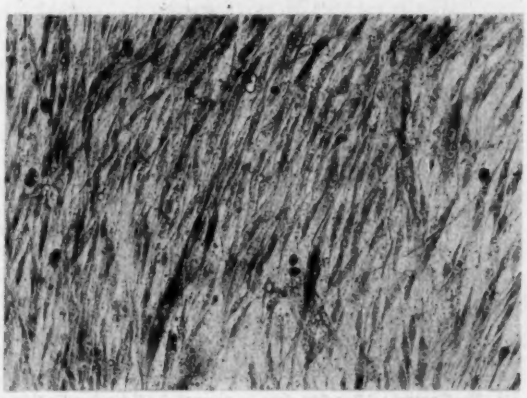

Fig. 25—After five days in normal medium plus cholesterol 30 mg. per 100 ml. in beta-lipoprotein solution.

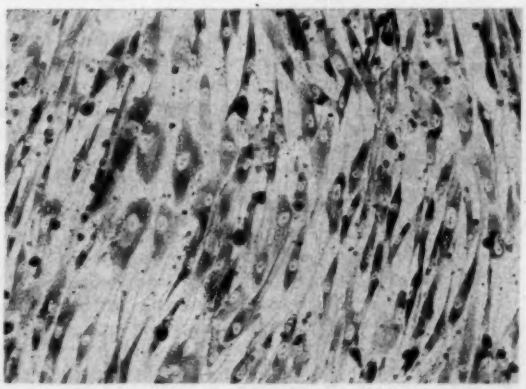

Fig. 26—After five days in normal medium plus cholesterol 50 mg. per 100 ml. in beta-lipoprotein solution.

acid are added simultaneously with the cholesterol, decreasing amounts of lipoid are deposited in the cells. The decrease is first evident when the concentration of added linolenic acid has been 0·005 mg. per 100 ml. (fig. 12), and is greater when it has been 0·05 mg. (fig. 13). Deposition is very slight when linolenic acid has been added at a concentration of 0·5 mg. per 100 ml. (fig. 14), and absent with a concentration of 1 mg. per 100 ml. (fig. 15).

Inhibition by Linolenic Acid and Potentiation by Stearic Acid of Tissue Lipoid Deposition when Cholesterol is added in Ethanol Solution.

The control cultures appear as before (figs. 16 and 17).

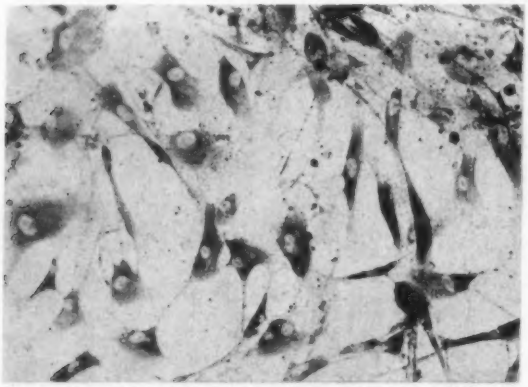

Fig. 27—After five days in normal medium plus cholesterol 70 mg. per 100 ml. in beta-lipoprotein solution.

Fig. 30—After five days in normal medium plus cholesterol 50 mg. per 100 ml. in beta-lipoprotein solution followed by five days in normal medium.

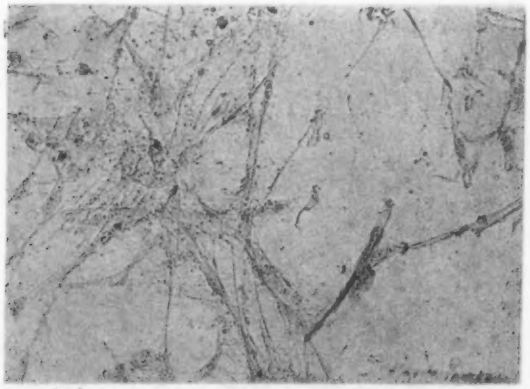

Fig. 28—Control. After five days in normal medium (aortic tissue donor J. C., serum donor W. R.). The same donors apply in figs. 29-31.

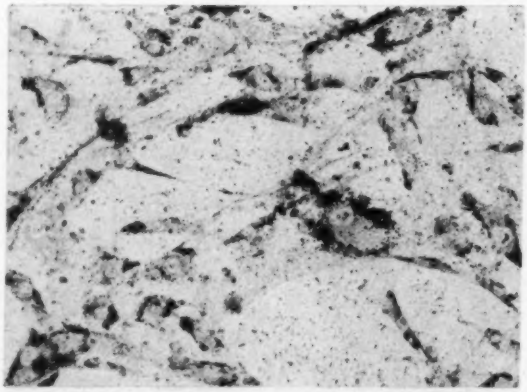

Fig. 31—After five days in normal medium plus cholesterol 50 mg. per 100 ml. in beta-lipoprotein solution followed by five more days in same solution.

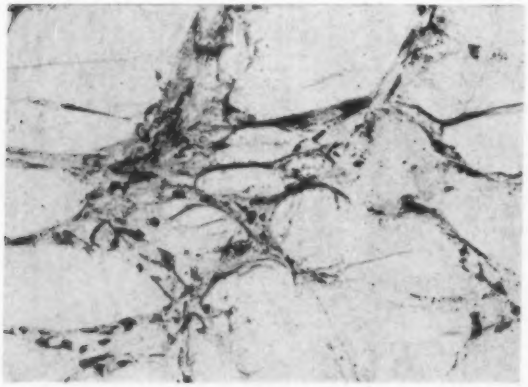

Fig. 29—After five days in normal medium plus cholesterol 50 mg. per 100 ml. in beta-lipoprotein solution.

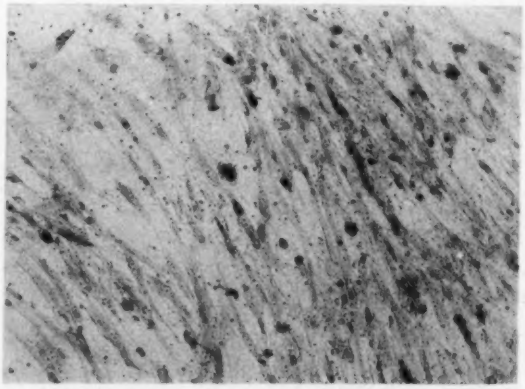

Fig. 32—Control. After six days in normal medium (aortic tissue donor A. D., serum donor W. R.). The same donors apply in figs. 33-35.

Lipoid is deposited in the cells to which cholesterol 3 mg. per 100 ml. has been added in ethanol (fig. 18). When linolenic acid has been added simultaneously at a concentration of 1 mg. per 100 ml., the intracellular deposition of lipoid is considerably decreased (fig. 19); but, when the corresponding saturated fatty acid, stearic acid, has been added in the same concentration of 1 mg. per 100 ml., the lipoid deposition is increased and the cells become very large (fig. 20). In control cultures, when linolenic acid has been added alone at a concentration of 1 mg. per 100 ml., the culture looks like the normal control (fig. 21), whereas in cultures to which stearic acid in the same concentration has been added alone the deposition of lipoid is very slightly increased (fig. 22).

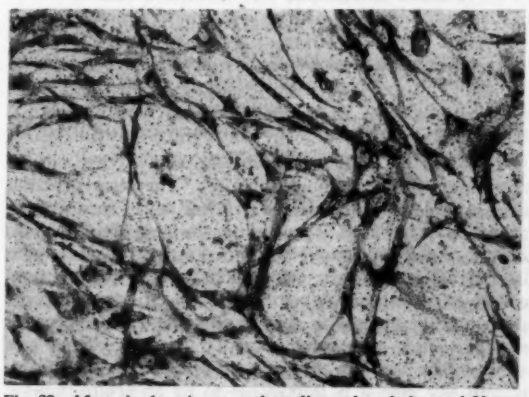

Fig. 33—After six days in normal medium plus cholesterol 50 mg. per 100 ml. in beta-lipoprotein solution.

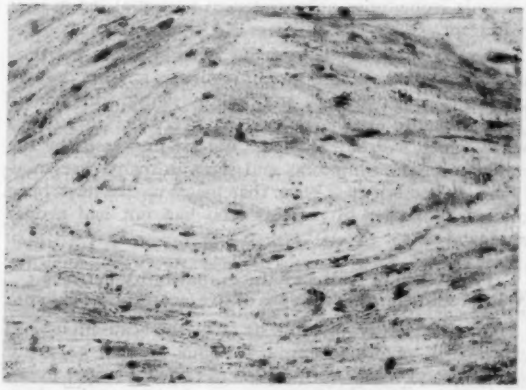

Fig. 34—After six days in normal medium plus cholesterol 50 mg. per 100 ml. in beta-lipoprotein solution and linolenic acid 1 mg. per 100 ml.

Fig. 35—After six days in normal medium plus cholesterol 50 mg. per 100 ml. in beta-lipoprotein solution and stearic acid 1 mg. per 100 ml.

Tissue Lipoid Deposition when Cholesterol bound to beta-Lipoprotein is Added

When beta-lipoprotein cholesterol is added, the intracellular deposition of lipoid is similar to that obtained by adding cholesterol in ethanol, but at a different range of concentration.

The control culture (fig. 23) resembles the culture containing cholesterol bound to beta-lipoprotein, at a concentration of 10 mg. per 100 ml. (fig. 24). Intracellular lipoid deposition first appears when the concentration of added cholesterol bound to beta-lipoprotein has been 30 mg. per 100 ml. (fig. 25).

At 50 mg. per 100 ml. intracellular lipoid deposition is clearly seen and is associated with an increase in the size of the cells (fig. 26). At this concentration of 50 mg. per 100 ml., added cholesterol bound to beta-lipoprotein produces about as much intracellular lipoid deposition as does added cholesterol in ethanol in a concentration of 3 mg. per 100 ml. When beta-lipoprotein cholesterol has been added in a concentration of 70 mg. per 100 ml., the deposition is even greater (fig. 27).

Reversibility of Tissue Lipoid Deposition Previously Induced by Cholesterol bound to beta-Lipoprotein.

The control culture appears as before (fig. 28). The intracellular deposition of lipoid induced by added beta-lipoprotein cholesterol at a concentration of 50 mg. per 100 ml. (fig. 29) is reversible. When such medium is replaced at five days with normal medium, the lipoid deposited in the cells almost all disappears by the end of five more days (fig. 30). In contrast, if the culture is fed again with medium containing added beta-lipoprotein cholesterol in the same concentration of 50 mg. per 100 ml., the lipoid deposited in the cells persists (fig. 31).

Inhibition by Linolenic Acid and Potentiation by Stearic Acid of Tissue Lipoid Deposition when Cholesterol is added bound to beta-Lipoprotein.

The control culture appears as before (fig. 32). When the beta-lipoprotein cholesterol has been added in a concentration of 50 mg. per 100 ml., lipoid is deposited in the cells (fig. 33). When linolenic acid 1 mg. per 100 ml. has been added simultaneously, then intracellular deposition of lipoid is almost completely inhibited (fig. 34). In contrast, when a similar concentration of stearic acid has been added with beta-lipoprotein cholesterol 50 mg. per 100 ml., much more lipoid is deposited in the cells, which become much larger (fig. 35).

Further Experiments.

Each of the steps in the above experiments has been performed from three to seven times with similar results. The morphological changes reported here are being investigated by chemical methods.

This technique makes possible the testing, at the level of intracellular lipoid deposition, of hypothetical mechanisms of human atherosclerosis, whether based on epidemiological evidence or on abnormally high levels of lipoid constituents of human blood-serum. The tech-

nique is now being applied to the study of human atherosclerosis.

Summary and Conclusions

Factors affecting the intracellular deposition of lipoid can be studied in human aortic cells in tissue-culture in a medium containing human blood-serum.

When cholesterol in ethanol is added to the culture medium, the amount of lipoid deposited in the cells is proportional to the amount of cholesterol added:

1. At a concentration of 1 mg. of added cholesterol per 100 ml., there is very little evidence of intracellular lipoid deposition.

2. At a concentration of 3 mg. per 100 ml., intracellular lipoid deposition regularly appears and is associated with an increase in the size of the cells.

3. At a concentration of 5 mg. per 100 ml., intracellular lipoid deposition is considerable and the cells are enormously increased in size.

Similarly, when cholesterol bound to beta-lipoprotein is added to the culture medium, the amount of lipoid deposited in the cells is proportional to the amount of cholesterol added:

1. At a concentration of 30 mg. of added cholesterol per 100 ml., there is very little evidence of intracellular lipoid deposition.

2. At a concentration of 50 mg. per 100 ml., intracellular lipoid deposition regularly appears and is associated with an increase in the size of the cells.

3. At a concentration of 70 mg. per 100 ml., intracellular lipoid deposition is considerable and the cells are enormously increased in size.

The intracellular deposition caused by adding cholesterol (whether in ethanol or protein-bound) disappears in five days if the medium containing the cholesterol is replaced by normal medium.

The intracellular deposition caused by adding cholesterol (whether in ethanol or protein-bound) is completely inhibited by simultaneous addition of linolenic acid (1 mg. per 100 ml.). It is increased by simultaneous addition of stearic acid (1 mg. per 100 ml.).

Thus, in tissue cultures of human aortic cells, deposition of lipoid can be induced by cholesterol, is reversible, can be inhibited by an unsaturated fatty acid (linolenic acid), and can be potentiated by the corresponding saturated fatty acid (stearic acid).

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"However impressive the difference between the hand of a cultured person and that of a prehistoric or primitive man may be externally, there can be no question of any fundamental difference. . . . Primitive man also works, touches, recognises and shapes objects, expresses his feelings, thoughts and desires with the help of the hand. If he did not do this he would not be a man. As the ape is not in a position to carry out these activities or to do so only in a very modest degree, his hand remains an organ of grasping, regardless of the degree of dexterity and mobility with which it is equipped and of the sort of movements which, through natural endowment, exercise and training, it may be capable. Between an organ of grasping and an expressive hand there is a large gap, which man alone has succeeded in bridging."—Prof. GÉZA RÉVÉSZ. *The Human Hand.* Translated by John Cohen. London, 1958.

THE ÆTIOLOGY, INCIDENCE, AND HEREDITY OF PRE-ECLAMPTIC TOXÆMIA OF PREGNANCY

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THE first difficulty which the student of this subject encounters is one of nomenclature. The term toxæmia is unsuitable for a disorder which has never been proved to be due to any kind of poisoning; the term pre-eclamptic should, strictly speaking, be applied only to patients who later develop eclamptic convulsions; and nowadays only a very small minority ever do so. Specific hypertensive disease of pregnancy is also an unsuitable title, because it seems clear that some patients develop œdema and albuminuria late in pregnancy without hypertension, and in any case it is impossible to fix an arbitrary level above which hypertension may be said to be present. We therefore reluctantly use the term pre-eclamptic toxæmia (sometimes abbreviated to toxæmia), because it is current.

The next difficulty is to define what is and is not pre-eclamptic toxæmia and to differentiate it from hypertension accompanying and complicating pregnancy. This difficulty we have tried to overcome in various ways, which will be specified. We are impressed by the mildness of the symptoms and signs in many cases now being diagnosed; it is clear that many would have been missed altogether in patients who had not had proper antenatal care.

Possibility of Antigenic Incompatibility between Mother and Fœtus as a Cause of Pre-eclamptic Toxæmia

No satisfactory hypothesis for the causation and mechanism of pre-eclamptic toxæmia has yet been put forward, and we do not propose to review the vast literature which always accumulates on any subject about which the medical profession is particularly ignorant. The object of this study is to seek evidence as to whether pregnancy toxæmia may be due to antigenic incompatibility between mother and fœtus.

Let it be supposed that the mother has a protein or other potential antigen represented by the gene E, which is not present in the fœtus, whose constitution, so far as this allele is concerned, is that of the homozygote ee. Clearly the mother must be heterozygous (Ee) because if she were homozygous (EE) she could not have a fœtus who was homozygous ee. Some of her potentially antigenic protein passes into the fœtus, who manufactures an antibody to it, which in turn is absorbed by the mother and damages the mother's kidneys, the condition being akin to rhesus incompatibility in reverse.

Such an explanation is attractive for the following reasons:

(1) It would explain why pregnancy toxæmia never takes place until the later months of pregnancy.

(2) It would explain the rapid recovery of the great majority of patients soon after the pregnancy is terminated, whether naturally or artificially.

(3) It would explain the fact that a woman may have toxæmia in some pregnancies but not in others, and that a woman who has had pre-eclamptic toxæmia is more liable than the general population to have it in a subsequent pregnancy.

(4) It would explain the increased incidence of pre-eclamptic toxæmia in twin pregnancies. For if the twins are identical a double dose of antibody may be produced, while if they are dissimilar there is twice the normal chance that one of them may be homozygous ee.

(5) It would explain why the fœtus does not have either albuminuria or kidney disease.

The hydatidiform mole might be, as Kalmus (1946) suggests, a case in which incompatibility worked both ways, the fœtus as well as the mother being adversely affected.

The theory of antigenic incompatibility as a cause of pregnancy toxæmia was put forward by Platt (1947), who was then unaware of the papers of Penrose (1946) and Kalmus (1946). Kalmus postulated the reverse situation—that the mother might be the homozygote and the fœtus the heterozygote. This seems to us to be less likely. It should be noted that, whereas an analogy may be drawn between this situation and rhesus incompatibility leading to erythroblastosis, we do not suggest that the condition has necessarily anything to do with blood-groups which are at present recognised or which may be discovered in the future.

If only one pair of genes, E and e, is commonly involved in the causation of pregnancy toxæmia in this country, the hypothesis can be examined by studying the incidence of pre-eclampsia in the relatives of women who have suffered from the disorder. The simplest case will be clear at a glance: if a woman, who for the sake of clarity we will call the proposita, has pre-eclamptic toxæmia, her mother could not have had pre-eclamptic toxæmia during the pregnancy in which the proposita was the fœtus. For the proposita must be Ee and, no matter what her mother's genetic constitution regarding this gene, the toxæmic configuration (Kalmus' term)—Ee/ee—cannot have existed. Similarly, a daughter (ee) arising from a toxæmic pregnancy cannot herself later have toxæmia. If, therefore, it can be shown that the mothers of toxæmic women never had pre-eclamptic toxæmia in the relevant pregnancies, and also that daughters arising from toxæmia pregnancies never have toxæmia in their own pregnancies, this evidence would go a long way towards supporting the hypothesis of antigenic incompatibility.

Furthermore, if the gene frequencies of E and e in the population can be calculated, the likelihood of various relatives of the proposita having pre-eclamptic toxæmia can also be calculated, and it will be seen from tables I and V that some of these relatives will be more, and others less, likely to have pre-eclamptic toxæmia than will the general population of women exposed to the risk of pregnancy.

If, however, there are several fairly common potential causes of antigenic incompatibility (which we might call factors E, F, and G), it is unlikely that statistical proof will be forthcoming, and the hypothesis must wait until more objective proofs of incompatibility are available. We are thus in the happy position of being perhaps able to bring evidence in favour of our explanation but being quite incapable of disproving it. In fact, the pilot trial here described does not bring to light any strong evidence in favour of the antigenic theory.

TABLE I—INCIDENCE OF PRE-ECLAMPTIC TOXÆMIA IN PROPOSITÆ AND THEIR RELATIVES ON THE ASSUMPTION OF AN ANTIGENIC INCOMPATIBILITY BETWEEN MOTHER (Ee) AND FŒTUS (ee)

Gene frequencies of E and e are p and q respectively, where $p+q=1$ (after Kalmus)

General incidence in the population	pq^2
Incidence in mother of proposita (proposita being fœtus)	0
" " " (in another pregnancy)	$\frac{1}{4}q$
" sisters of propositæ	$\frac{1}{4}q(1+pq)$
" wives of brothers of propositæ	$\frac{1}{4}pq(1+2q)$
" mothers-in-law (husband being fœtus)	pq
" " " (in another pregnancy)	$\frac{1}{4}pq(2+q)$
" husband's sisters	$\frac{1}{4}pq(1+2q)$
" husband's brothers' wives	$\frac{1}{4}pq(1+3q)$
" proposita in another pregnancy (having had a toxæmic one)	$\frac{1}{4}(1+q)$

Table I, which has been compiled with the help of Dr. Kalmus, shows the relative frequency of pregnancy toxæmia in the general population and in relatives of toxæmic women, assuming a frequency for genes E and e of p and q respectively. The next step—the calculation of gene frequencies—depends on the ascertainment of the incidence of pre-eclamptic toxæmia in the general population.

General Incidence of Pre-eclamptic Toxæmia

Of the incidence of toxæmia in the general population surprisingly little is known. Most of the existing records are from highly selected hospital populations. The only papers known to us which attempt to avoid this bias are that by Gemmell, Logan, and Benjamin (1954), and the obstetric survey of the South West faculty of the College of General Practitioners (1957).

Gemmell et al. estimated the number of cases of pre-eclamptic toxæmia in Liverpool in 1951, on the assumption that all such cases would be sent to a hospital or other maternity unit. They compared this figure with the total number of births in Liverpol in the same year. There are obviously some potential fallacies in their method, and these workers admit that they could not separate cases of hypertension complicating pregnancy from cases of pre-eclamptic toxæmia. Like other students of this subject, they find that pre-eclamptic toxæmia is commoner in first pregnancies (8·5%) than in subsequent pregnancies (4·2%). They estimate the total chance of any parous woman developing pre-eclamptic toxæmia at some time during her childbearing life at about 13%.

The obstetric survey from the College of General Practitioners (1957) also does not distinguish between pre-existing hypertension and pregnancy toxæmia. It records an incidence of hypertension (140/90 or more) in 16% of primiparæ and 9% of multiparæ. Of these hypertensives, 43% of primiparæ and 31% of multiparæ also had albuminuria—i.e., 7% and 3% approximately of total pregnancies. The interesting comment is made that of these hypertensive albuminuric cases only 38% of primiparæ and 30% of multiparæ were delivered in specialist hospitals. It is not stated how many were delivered at home, and the usual practice in this respect may be very different in the South West of England from that which would obtain in a city like Liverpool; but the survey suggests that the method of Gemmell et al. (1954) may miss some home deliveries of pre-eclamptic patients.

In an attempt to make our own estimate of the incidence of toxæmia in an unselected population, we sent a questionary to the 716 men and women who graduated in medicine in Manchester University in 1946–55. We admit of course that this series is not unselected so far as intelligence and social class are concerned, but we know of no evidence that pregnancy toxæmia is determined by such factors. The group is also selected as regards age; but it seemed to us that women doctors who have themselves had babies, and male doctors whose wives have had babies, should be the most reliable witnesses possible as to whether pregnancy toxæmia had occurred or not.

TABLE II—FATE OF QUESTIONARIES

No. of graduates in medicine 1946–55	716
No. untraceable (letters returned by Post Office)	25
No. written-off (see text)	6
No. of intermarriages known	36
No. of unmarried siblings deleted (see text)	4
No. not replied after 2nd letter	72*
No. of replies analysed	573
Total	716

*Some of these may be women known to us by their maiden name whose husbands have replied.

The questionary asked: whether the "wife" (i.e., either the woman doctor or the doctor's wife) had had pregnancies; if so, how many and whether they were complicated by toxæmia; and if so, whether hypertension, œdema, and albuminuria were present or only some of these phenomena. The witnesses were asked similar questions about pregnancies of the wife's mother, her sisters, her brother's wives, her mother-in-law, her husband's sisters, and her husband's brothers' wives.

Table II shows that, of 716 questionaries, only 573 are available for analysis. In 36 instances this is due to intermarriage between graduates; clearly in such cases husband and wife can only give the same information.† Again, when unmarried graduate siblings exist, they can give no additional information about their families; but in the case of married siblings—e.g., two brothers, both married and having families, and both graduates—both have been included, even though this leads to a very minor degree of duplication of some of the data. Cases described as written-off include several people who were of African or Asiatic race, or who were adopted children, and could give no information of value. Half-brothers and half-sisters, of whom there were very few, were not counted as brothers and sisters. Abortions, and pregnancies still unfinished at the time of completing the questionary, were not counted as pregnancies.

Table III shows the incidence of pregnancy in the "wives" of the series. This is the table which should give the most accurate information, because these pregnancies, nearly all of which occurred within the last ten years, will have been most carefully observed. It will be seen that altogether 290 "wives" were at risk in the sense of having had at least one pregnancy, and among these the incidence of toxæmia in the first pregnancy is 11·7%; but this may be somewhat exaggerated; and here we come at once into one of the difficulties of the

TABLE III—WOMAN GRADUATE OR WIFE OF GRADUATE

No. of 1st pregnancies	290	Toxæmic	34*	(11·7%*)
,, ,, 2nd ,,	153	,,	8*	(5·2%*)
,, ,, 3rd ,,	39	,,	1	(2·6%)
,, ,, 4th ,,	8	,,	1	(12·5%)
,, ,, 5th ,,	2	,,	0	
,, ,, 6th ,,	1	,,	0	

*Reduced to 29 (10·0%) and 6 (4·0%) respectively (see text).
Number toxæmic only in 2nd or later pregnancy = 3
Total wives having toxæmia (corrected) = 32 (11%)

subject, because of the 34 cases of toxæmia occurring in first pregnancies no albuminuria was reported in 16. On the other hand, 11 of these 16 women had both œdema and hypertension (a rise of blood-pressure significantly above that observed earlier in the pregnancy) so it seems reasonable to estimate the incidence of toxæmia as 29 cases (10%). This figure is, as one would expect, somewhat higher than that of Gemmell et al. (1954) and that from the College of General Practitioners (1957). The number of women having toxæmia in second pregnancies is 4%. This might be a false figure if women having had one toxæmia pregnancy showed a strong reluctance to embark on a second pregnancy. Such, however, was not the case. Of 290 women who had had first pregnancies 153 (53%) had had second pregnancies. Of 34 women who had had toxæmic first pregnancies 15 (44%) have already had second pregnancies.

We see from table I that the general incidence of pre-eclamptic toxæmia in women exposed to the risk of pregnancy should be pq^2, where p is the gene frequency of E, and q the gene frequency of e ($p + q = 1$), assuming that all women in whom this maternal and fœtal incompatibility exists will develop signs of toxæmia. All observers have found toxæmia to be more common in

TABLE IV—RELATIVES OF WOMEN GRADUATES OR OF MEN GRADUATES' WIVES

Mothers:			
1st pregnancies	458*		
Pregnancy history unknown	14		
	444		
Toxæmia in 1st pregnancy		15	(3·4%)
,, ,, subsequent pregnancy only		9	(2·0%)
		Total	5·4%
Sisters:			
1st pregnancies	167		
Toxæmia in 1st pregnancy		10	(6·0%)
,, ,, subsequent pregnancy only		3	(1·8%)
		Total	7·8%
Wives of brothers:			
1st pregnancies	124		
Toxæmia in 1st pregnancy		11	(8·9%)
,, ,, subsequent pregnancy only		5	(4·0%)
		Total	12·9%
Husbands' mothers:			
1st pregnancies	516*		
Pregnancy history unknown	9		
	507		
Toxæmia in 1st pregnancy		17	(3·3%)
,, ,, subsequent pregnancy only		8	(1·5%)
			4·8%
Husbands' sisters:			
1st pregnancies	182		
Toxæmia in 1st pregnancy		10	(5·5%)
,, ,, subsequent pregnancy only		5	(2·7%)
		Total	8·2%
Husbands' brothers' wives:			
1st pregnancies	178		
Toxæmia in 1st pregnancy		13	(7·3%)
,, ,, subsequent pregnancy only		4	(2·2%)
		Total	9·5%

*These figures are less than 573 because of the unmarried members of the series.

first pregnancies than in subsequent pregnancies; therefore one must assume that there is some factor whch protects the mother in subsequent pregnancies, and we will take the incidence in first pregnancies as our basis for the calculation of gene frequencies. If pq^2 equals 10% or 0·1, there are two figures which we may take for the approximate values of p and q—either $p = 0{\cdot}59$, $q = 0{\cdot}41$ or $p = 0{\cdot}13$, $q = 0{\cdot}87$.‡

Incidence of Toxæmia in Relatives of Toxæmic Women

Table IV shows the observed incidence of toxæmia in relatives of all the "wives" (i.e., not merely the toxæmic ones), and, before analysing these more carefully, it can be seen at first glance that relatives of the same generation (i.e., sisters, brothers' wives, sisters-in-law, and wives of brothers-in-law) have an incidence of toxæmia which approaches that of the "wives" themselves, whereas members of the previous generation (i.e., mothers and mothers-in-law) have a considerably lower incidence. This we feel is much more likely to be due to failure of diagnosis through lack of antenatal

† The role of this Medical School as a matrimonial agency is an interesting side-issue of this inquiry.

‡ Note that theoretically the greatest possible value of pq^2 is 14·81% when $p = 0{\cdot}33$ (Kalmus 1946).

TABLE V—INCIDENCE OF TOXÆMIA IN 1ST PREGNANCIES OF RELATIVES OF TOXÆMIC WOMEN

—	Expected incidence * (see table I)		Graduate series		Portsmouth series		Manchester series		Manchester and Portsmouth series	
	If q = 0·41 %	If q = 0·87 %	Incidence	Total at risk	Incidence	Total at risk	Incidence	Total at risk	Incidence	Total at risk
General population	10	10	29	290	..	..	..	..	..	..
Mother (proposita being fœtus)	0	0	0	48	2	38	1	38	3	76
Mother (another child)	10	22	1 (25%)	4	2 (20%)	10†	0	6†	2	16†
Mother-in-law (husband being fœtus)	24	11	4 (7%)	55	0	36	1 (3%)	30	1 (2%)	66
Mother-in-law (another child)	15	8	1 (17%)	6	0	2†	0	1†	0	3†
Sister	13	24	2 (8%)	23	11 (28%)	40	4 (8%)	46	15 (17%)	86
Brother's wife	11	8	4 (17%)	24	1 (3%)	32	1 (3%)	31	2 (3%)	63
Husband's sister	11	8	5 (14%)	35	3 (6%)	48	0	25	3 (4%)	73
Husband's brothers' wife	13	10	3 (10%)	31	0	21	0	26	0	47
Proposita herself in 1st pregnancy (subsequent pregnancy being toxæmic)	35	47	17 (53%)	32	..	..	..	..	..	..

* On the assumption that toxæmia develops in all cases where the genetic situation allows it to.
† Some of these figures are very small because the birth order was not ascertained.
In the Portsmouth series there are 2 pairs of sisters in which both are counted as propositæ.

care than to any factor causing an increased incidence of toxæmia in the present generation.

Table v sets out the incidence of toxæmia expected in relatives of women who have actually had toxæmia themselves, based on a value for q of 0·41 or of 0·87, and calculated from table I. It will be seen that, in either case, the incidence of toxæmia in the mother of a toxæmic woman should be 0 in the relevant pregnancy, as we have already remarked. If q = 0·87, the incidence of toxæmia in the mother's other pregnancies should be high, as should be the incidence of toxæmia in the sisters of toxæmic women. If q = 0·41, the incidence of toxæmia in the mothers-in-law of toxæmic women during the birth of the toxæmic woman's husband should be high, and with either gene frequency the chances of toxæmia occurring again in a subsequent pregnancy are very high indeed.

Table V gives the actual incidence of toxæmia in the relatives of all women in the graduate series who have had toxæmia themselves. If the "wives", their sisters, and their husbands' sisters are included, there are altogether 54 women who have had toxæmia and whose mother's history as regards toxæmia is known and recorded. Of these 54, 3 had mothers who were also affected by toxæmia,* and in none of these 3 cases was the mother affected during the pregnancy from which the toxæmic daughter was born.

Conversely, there are 12 parous women of the present generation whose mothers had toxæmia when they were born, and in no case have these 12 daughters had toxæmia in their own pregnancies. There is thus no exception to the rule we have stated, but the figures are too small for the finding to be significant. The prediction, that the chances of pre-eclamptic toxæmia occurring again in a subsequent pregnancy are high, is of course amply justified by this table, as we would have expected from what is already known. The figures for the incidence of pregnancy toxæmia in other relatives are probably not significantly different from the normal range.

To put the hypothesis further to the test we have taken family histories from 100 women in hospital or in antenatal clinics who have had pre-eclamptic toxæmia: 50 of these were examined by A. S. and are called the Portsmouth series; and 50 were examined by R. P. and are called the Manchester series. In this part of the work we felt that selection was desirable, provided women were not selected simply because they had an interesting family history. We therefore decided in advance on the examination of a consecutive series who should fulfil the following criteria:

(1) There must be antenatal records showing clearly that the blood-pressure had remained normal and the urine free from albumin in the earlier stages of the pregnancy.

(2) The women must have later developed albuminuria and either œdema or hypertension or both. Hypertension was not strictly defined but was taken to mean rises of blood-pressure significantly above those recorded earlier in the pregnancy. In most cases there was a clear and fairly sudden onset of these signs.

Naturally the ascertainment of family histories from patients in this way is full of difficulties, and the data may not be very accurate. In the Portsmouth series are two pairs of sisters—i.e., each of the sisters had pregnancy toxæmia and has been counted in the series. Table v shows the incidence of pregnancy toxæmia, so far as we could ascertain it, in the first pregnancies of the relatives of these patients. We do not think there is very much that is significant in this table except that the incidence of toxæmia in the sisters of toxæmic women appears to be very high, and there are 3 cases in which the mother had pregnancy toxæmia in the pregnancy from which the proposita arose—in other words, there are 3 cases which count clearly against our hypothesis in its simplest form:

(1) One of these is not very impressive, in that the mother simply said that she had kidney trouble with her pregnancy.

(2) The second said that she had kidney trouble with both pregnancies and had much œdema.

(3) The third, an intelligent woman in the Manchester series, said that her mother had "albumin" badly when she was born and again in her other pregnancies; and in the pregnancy from which the proposita was born the mother had to rest and was taken to hospital; she had a high blood-pressure with each pregnancy.

Within the limitations of this kind of inquiry this seems to be evidence which we are bound to accept, and we therefore did not extend the series any further.

In accepting even a single case in which the daughter from a toxæmic pregnancy has toxæmia in one of her own pregnancies we have to discard the simple hypothesis proposed above. It is nevertheless possible that some more complex system of antigenic incompatibility may underlie this condition; and, if so, it would be expected to cause an irregular incidence of toxæmia among the relatives of toxæmic women, just as the simple theory would—some relationships showing an incidence raised

* Not all of these pregnancies are recorded in table v, which shows only first pregnancies.

above that in the general population, and others depressed below it. We have therefore examined our data for evidence that differences in observed frequency are greater than might be expected to arise by pure chance. There is some slight indication that this may be so.

We have considered the incidence of toxæmia in first pregnancies of sisters of propositæ, brothers' wives, husbands' sisters, and husbands' brothers' wives. To obtain adequate numbers for statistical treatment the Manchester, Portsmouth, and graduate series were combined; and where there is any duplication among subjects, as with the two pairs of sisters mentioned previously in the Portsmouth series, only one individual has been counted. The result of the analysis is: χ^2 8·23, $n=3p=0{\cdot}040$.

A slightly more significant result is obtained if we consider also the mothers of propositæ and of their husbands both in the pregnancies when the proposita or her husband was the fœtus and in other pregnancies. These cases correspond to rows 1–4 of table V, but to obtain adequate number we have had to consider all pregnancies whose histories we could obtain, not merely the first, and also to combine "mother (proposita being fœtus)" with "mother-in-law (husband being fœtus)". It happens that the frequency of toxæmia was about the same in these two classes; so no variability is obscured by combining them. This group of mothers and mothers-in-law cannot, of course, be compared directly with the groups of sisters and sisters-in-law of propositæ, first because we believe the probability of diagnosis to be much smaller in the elder generation, and secondly because we have considered all their pregnancies and not only the first. Considered separately the group of mothers and mother-in-law give $\chi^2=3{\cdot}97$, n=2, and combining for the two groups we have $\chi^2=12{\cdot}20$, n=5, P=0·032.

In the course of the inquiry we came across three histories which seem to be of interest:

(1) In one case a husband's first wife died of eclampsia in her only pregnancy: his second wife had toxæmia in each of two pregnancies. (2) In another case the husband's brother's wife had toxæmia, but she had been married before and had no toxæmia in two pregnancies from her first husband. (3) A third woman had two normal pregnancies and then changed her husband and had toxæmia in her third pregnancy.

ABO and Rh blood-groups were recorded in 97 of these 100 cases. Their distribution does not appear to differ significantly from that in the general population. Although they are irrelevant to our paper, we record them in table VI.

TABLE VI—BLOOD-GROUPS OF 97 TOXÆMIC WOMEN

O	A	B	AB	Rh+	Rh−
39	44	10	4	78	19

Summary and Conclusions

This investigation was designed to test the hypothesis that antigenic incompatibility between mother and fœtus is the cause of pregnancy toxæmia. This hypothesis would explain many of the peculiar features of this condition.

If a single antigenic factor were at work, evidence in favour of the hypothesis could be obtained by investigating the incidence of toxæmia in the relatives of toxæmic women.

The result of this investigation strongly suggests that if incompatibility exists it is not due to a single factor, but does not rule out the possibility that several factors may be at work.

In the course of the investigation we studied the general incidence of toxæmia in 573 women medical gaduates and wives of medical graduates, and their relatives.

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ACCIDENTAL HYPOTHERMIA

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THE body temperature in mammals is controlled by the hypothalamus, which contains separate centres for heat loss and conservation. The heat-conservation centre lies in the posterior hypothalamus and is activated by stimuli from cold receptors in the skin and by fall in temperature of the blood perfusing it. Efferent stimuli cause cutaneous vasoconstriction, increased muscle-tone, and shivering, and both vascular and muscular responses are potentiated by adrenaline release. In extreme cold the mechanism may be inadequate, and is assisted by the use of extra clothing and external warmth, without which cooling is excessive. This hazard is more likely at the extremes of life and during illness, sedation, or anoxia, when the physiological responses are impaired. The severity of the resulting hypothermia depends largely on the amount of tissue insulation, which shows much individual variability (Pugh and Edholm 1955).

As cooling progresses an initial rise in blood-pressure and heart-rate is succeeded by hypotension, with a fall in plasma-volume, and bradycardia—probably due to a direct effect on the pacemaker. Peripheral pulses disappear, the circulation-time increases, and at about 86°F (30°C) atrial fibrillation or other arrhythmias may begin. Shivering continues until 91°–86°F (33°–30°C) is reached, when it is succeeded by intense muscle rigidity; this disappears at about 81°F (27·2°C). At 86°F (30°C) consciousness becomes clouded, and about 77°F (25°C) the blood-pressure falls abruptly and the patient dies from cardiac failure (Alexander 1946, Crismon and Elliott 1947).

Artificial hypothermia has been studied in its surgical and therapeutic use, and immersion hypothermia is a well-recognised hazard following shipwreck; it was common in airmen forced down in the sea during the late war (Wayburn 1947). In clinical medicine hypothermia is uncommon and may pass unrecognised when it complicates severe illness which modifies its features.

It has been described in alcoholism (Reincke 1875) and the lowest recorded temperature with survival (18°C) was in a young alcoholic woman following exposure (Laufman 1951). Hypothermia is an uncommon but well-recognised complication of hypopituitarism (Sheehan and Summers 1952) and myxœdema when retarded metabolism facilitates its appearance (Summers 1953, Le Marquand et al. 1953, Malden 1955, Marshall and McCaughey 1956). It has been reported in the newborn, in whom the homœothermic mechanism is unstable (Mann 1955, Mann and Elliott 1957), and as a complication of chronic illness, cerebral lesions, coma, and shock (Briggs 1950, Abrahams 1954, Eason and Macnaughton 1956).

Four cases are here reported (of senility, myocardial infarction, paraplegia, and diabetic coma) in which hypo-

thermia developed, with rectal temperatures of 80–90°F (26·7°–32·2°C).

Case-reports

Case 1.—A man, aged 86, who lived alone and had become increasingly infirm, fell in his unheated room, and lay there lightly clothed until next morning, when he was admitted. The minimum night air temperature was 43·6°F (6·5°C).

He was thin, dirty, and lice-ridden. His skin was pale, with collapsed veins, and was very cold to the touch. Body hair was scanty and there was moderate testicular atrophy. He was semiconscious and groaned hoarsely when disturbed, but did not speak. He obeyed commands to move his limbs with a very slow, incomplete response. Striking muscle rigidity was present with no shivering, and abdominal and leg reflexes were absent, though those in the arms were just present. The mouth temperature did not record on a clinical thermometer reading from 95°F (35°C); there was sinus bradycardia (rate 36 a minute), a blood-pressure of 150/70 mm. Hg, and a respiration-rate of 13 a minute.

He was warmed with blankets and hot-water bottles, but after six hours had not improved; the rectal temperature was found to be 82°F (27·8°C). He was then placed in a bath initially at 98°F (36·7°C), increasing to 106°F (41·1°C). In an hour his rectal temperature rose to 90°F (32·2°C) and he was transferred back to bed (fig. 1). The clinical response was dramatic, with recovery of speech and spontaneous movement, though he remained mildly confused for some hours. The muscle rigidity disappeared, but no shivering was seen. Antibiotics and a single injection of cortisone (100 mg. intramuscularly) were given after warming, and hypotension (see fig. 1) was treated with repeated intramuscular doses of mephentermine ('Mephine') 30 mg. with satisfactory but temporary relief. The blood-pressure eventually stabilised at 120/80 mm. Hg by the third day. Retention of urine required repeated catheterisation. Electrocardiograms showed ischæmic changes only; a leucocytosis accompanied recovery, and the 17-ketosteroid excretion was 1·6 mg. per twenty-four hours; other investigations were not notable. In the fifth week he was well enough for suprapubic prostatectomy and later walked. In the ninth week he had a pulmonary embolus and then deteriorated, dying twelve weeks after admission from pulmonary infection.

At necropsy no other lesion was found. The hypothalamus and all endocrine glands appeared normal. Coronary atherosclerosis was seen without myocardial infarction.

In old age the temperature is often low, and Howell (1944) reported a mean oral reading of 97·2°F (36·2°C) over the age of 80. He noted that readings of 95°F or below were very unusual in health but not uncommon in illness. These features were well shown in this patient, whose temperature on recovery was 98°F. In the first and last weeks it was often 95°–96°F; it fell to this level after prostatectomy and to 94°F after pulmonary embolism. In this case it seemed that senility had blunted the mental and physiological responses to cold, and that cooling was favoured by emaciation.

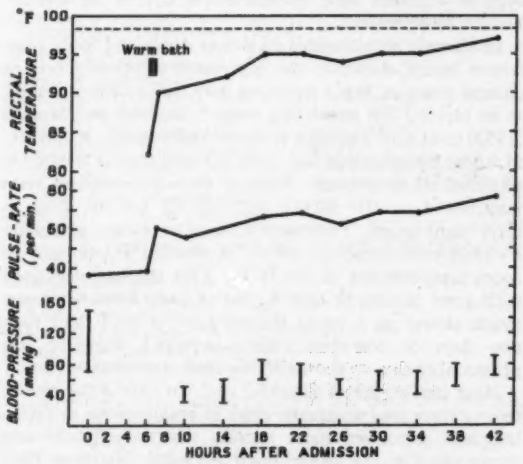

Fig. 1—Progress in case 1.

Case 2.—A man, aged 71, previously in good health, lost consciousness suddenly on the morning of Feb. 15, 1955, a particularly cold day (air temperature at 9 A.M. 34·0°F [1·1°C]) and lay lightly dressed in an unheated room until he was discovered nine hours later.

On examination he was thin, stuporose, and pale. The skin was very cold, with collapsed veins, and generalised muscle stiffness was found without shivering. Arm reflexes were reduced and leg reflexes were absent.

The initial oral temperature was recorded by a clinical thermometer as 95°F (35°C), and he had a sinus bradycardia (rate 36 a minute), a blood-pressure of 130/70 mm. Hg, and a respiration-rate of 22 a minute. There were no other abnormal signs. Heavy glycosuria, mild acetonuria, and albuminuria were found, and the blood-sugar was 158 mg. per 100 ml. Electrocardiograms showed ischæmic changes only.

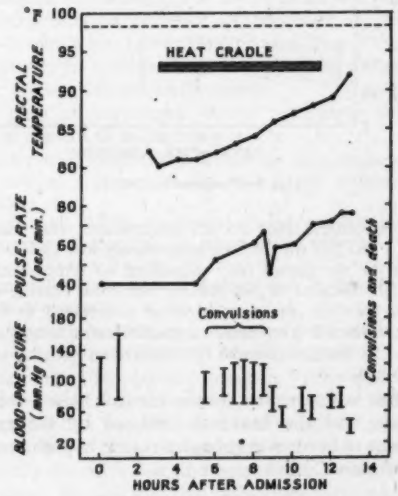

Fig. 2—Progress in case 2.

Three hours after admission there was no improvement; his rectal temperature was 80°F (26·7°C), and warming with a heat cradle was started (fig. 2). His temperature rose slowly and progressively over the next eight hours, the rise averaging 1°F an hour. During this period he had two convulsions, and after the second he lapsed into coma; the cradle was removed. Despite this his temperature continued to rise, but his condition deteriorated with deepening coma and increasing hypotension until his death fourteen hours after admission, following a third convulsion.

Necropsy showed advanced coronary atherosclerosis with almost complete obstruction of the left coronary artery 1½ in. from its origin, and total obstruction of the right coronary artery by recent ante-mortem thrombus leading to infarction. The pituitary gland was normal histologically, but the hypothalamus was not examined.

In this patient the sudden loss of consciousness is attributed to cardiac syncope following acute coronary occlusion, with hypothermia from exposure.

Case 3.—A woman, aged 43, was admitted, after a car accident, with a fracture-dislocation of the cervical spine at c5–6, causing acute paraplegia which proved permanent.

She was nursed in the open ward and burns on the buttocks, sustained in the accident, were treated by exposure. Five days after admission her temperature could not be recorded with the ordinary clinical thermometer, and she complained of mild subjective coldness, with no shivering or disturbance

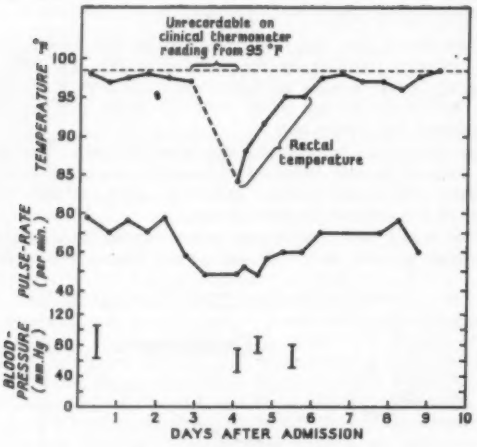

Fig. 3—Progress in case 3.

of consciousness. Her rectal temperature was then 84°F (28·9°C). At this time the air temperature was 13°F below the average for the month (day maximum air temperature 57°F [13·9°C]). Because of her sensory loss local heating was not thought suitable; she was therefore transferred to a heated sideroom where her temperature gradually rose to normal levels (fig. 3). No further episodes occurred when she later returned to the ward.

In this case homœothermic control below the lesion was lost, and the heat-loss incurred by the exposure treatment of burns was enough to cause hypothermia even in the summer.

Case 4.—A woman, aged 44, was admitted in diabetic coma on a day when the 9 A.M. air temperature was 59°F (15°C). She was deeply unconscious and dehydrated, with acidotic breathing. Her skin was cold and pale, and the superficial veins were much collapsed. Slight shivering was seen, but there was no muscle rigidity. The pulse-rate was 80 a minute, blood-pressure 60/30 mm. Hg, and respiration-rate 22 a minute. The rectal temperature was 90°F (32·2°C). Heavy glycosuria and acetonuria was found with a blood-sugar of 1350 mg. per 100 ml. and an alkali reserve of 7 mEq. a litre. She was resuscitated with intravenous fluids, glucose, and insulin, and noradrenaline for her hypotension. It was decided to treat the hypothermia by slow warming, and she was covered by a single blanket and allowed to rewarm spontaneously in a room temperature of 70°F (21°C). Eight hours after admission her temperature had risen to 98°F (36·7°C) at a rate of 1°F per hour.

In this case the hypothermia resulted from heat-loss during coma and contributed little to the clinical picture, though increasing doses of noradrenaline were needed to control the hypotension as her temperature rose.

Discussion

These cases show the variety of conditions in which hypothermia may develop, and it is perhaps surprising that it is not commoner in the winter months.

There may easily be delay in diagnosis because of reliance on the standard clinical thermometer; this was so in the first three cases. Thus in case 2 the temperature was recorded mistakenly as 95°F (35°C) and in the others the temperatures were charted as unrecordable. There were delays of six and three hours respectively in cases 1 and 2 before the depth of hypothermia was appreciated, and in case 3 the bradycardia on the previous day suggests that hypothermia was present then. This difficulty was noted by Sheehan and Summers (1952), and is readily avoided by the use of a low-reading rectal thermometer whenever the ordinary clinical instrument fails to register. The absence of shivering may contribute to this delay. None of the present patients shivered except case 4, and she only slightly. Shivering is an unreliable sign in accidental hypothermia because it is abolished by many drugs and by anoxia and does not occur in severe cases.

In the first two cases the clinical features were striking, with pallor and muscle rigidity resembling rigor mortis. Both had bradycardia, collapsed veins, and a normal blood-pressure; these are remarkable features in the presence of a large myocardial infarct (case 2). In contrast, case 3 had a combination of bradycardia and hypotension, the latter due to vasomotor paralysis.

Consciousness was undisturbed in case 3 at 84°F (28·9°C), whereas case 1 at 82°F (27·8°C) was semiconscious and case 3 at 80°F (26·7°C) was stuporose, though cerebral anoxia probably contributed to this.

Hyperglycæmia and glycosuria are reported in hypothermia and may have caused the findings in case 2.

Arrhythmias developed in none of the patients, and electrocardiograms did not show the specific " injury potential " of hypothermia (Osborn 1953).

The treatment of accidental hypothermia varies with its duration and may be either rapid or slow rewarming. Moderate warming should not be used, since this may release vasospasm without sufficient warming of blood. Chilled blood returns to the heart, lowering the central temperature still further, and in critical cases death may result from cardiac arrest soon after starting treatment (Burton and Edholm 1955).

In acute hypothermia of rapid onset and less than twelve hours' duration, such as immersion hypothermia, rapid warming is recommended. Burton and Edholm suggest a warm bath at 113°F (45°C), or an electric blanket may be used.

In chronic hypothermia of slower onset and more than twelve hours' duration, the type most commonly met in clinical practice, rapid warming may lead to hypotension, as in case 1. To avoid this danger Tallbott and Burton (1952) used slow warming to resuscitate a group of patients in whom hypothermia had been induced for the treatment of advanced neoplasms. Some of these patients had been maintained at 77°–80·6°F (25°–27°C) for as long as forty-eight hours. They were allowed to rewarm gradually by their own metabolic efforts at about 1°F per hour in room temperatures of 70–75°F. This method was used with good results in case 4, but in case 3 recovery was much slower in a room temperature of 65°F and took two days to complete. This impaired response was presumably due to the defective heat conservation.

Heat cradles are of doubtful use. In case 2 the rise in temperature was no greater than in spontaneous rewarming, and continued more rapidly when the cradle was removed. On the other hand in some instances they give excessive heat, leading to increasing shock (Gavey

1941, Grant and McMichael 1942). Their effect varies considerably, and they should be avoided since moderate warming with its attendant dangers could result.

Case 2 presented a difficult problem as he deteriorated despite a slow rate of warming. Murray and Bruce (1955) have used hypothermia in the treatment of severe shock due to postpartum hæmorrhage, and thought improvement was due to reduction in tachycardia and tissue oxygen requirements. Their patient also had convulsions during warming. Thus in case 2 accidental hypothermia itself might have protected against shock and could perhaps have been continued in the hope that the myocardium would recover enough to meet the increased demands of euthermia. Deterioration on slow rewarming may therefore be an indication to continue cooling as a temporary therapeutic measure.

In hypothermia there is evidence of adrenal damage and depletion of hepatic and cardiac glycogen, which may lead to heart-failure even at relatively high temperatures (Grosse-Brockhoff 1950). Cortisone, intravenous glucose, and digitalis may therefore be given during recovery.

Summary

Four cases of accidental hypothermia are reported. The primary conditions were senility, myocardial infarction, acute paraplegia, and diabetic coma.

The diagnosis may be overlooked if a low-reading rectal thermometer is not used whenever the ordinary clinical thermometer fails to register.

In treatment moderate warming should not be used, owing to the risk of increasing hypothermia and death from cardiac arrest. In acute hypothermia rapid warming is indicated; but in chronic hypothermia this may cause hypotension, and spontaneous, slow warming by the patient's metabolic processes is best. In circumstances where metabolism is depressed or heat conservation defective this may be insufficient, and some external warming is required.

In one case accidental hypothermia may have protected against shock. Deterioration during slow warming may be an indication to continue hypothermia.

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MITRAL VALVOTOMY AND PREGNANCY

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DESPITE advancing knowledge and improvements in medical care pregnancy in patients with severe mitral stenosis remains hazardous, mainly because of pulmonary œdema (Jones 1951).

The surgical relief of the stenosis offers a new approach, both in rendering patients fit to undergo a pregnancy hitherto possibly deemed inadvisable and in the relief of symptoms during pregnancy. It is, however, generally accepted that valvotomy rarely produces a valve of normal size, and objective evidence of improvement may be absent despite a good functional result. Since the burden of pregnancy is considerable, there may be danger even after a functionally good valvotomy.

The place of valvotomy during pregnancy has also been the subject of controversy:

Burwell (1954) stated that it should be reserved for cases in which medical management has failed and termination is inadvisable.

Glover et al. (1955) considered that pregnancy increased the operative risk but that, in severe cases, valvotomy should be preferred to termination.

Mulcahy (1954) felt that pregnancy was, in fact, an added indication for surgery.

This paper is based upon a study of 27 women with mitral stenosis, of whom 12 were operated on during pregnancy and 15 underwent pregnancy after a successful valvotomy. From our experience and from the published details of 89 other patients submitted to valvotomy during pregnancy we find that pregnancy does not appear to increase the operative risk, and operation is rarely followed by abortion. We also find that difficulties may be encountered in pregnancies following apparently successful valvotomy.

Material and Methods

The material consisted of 27 patients who had mitral stenosis and were attending either the department of cardiology at the Royal Infirmary or the thoracic centre at Park Hospital, Manchester. All were examined in the usual manner clinically, radiologically, and electrocardiographically and allotted American Heart Association functional gradings. Active infection was excluded as far as possible by clinical examination, a routine blood-count, and estimation of the erythrocyte-sedimentation rate (Wintrobe). Only 2 women were submitted to cardiac catheterisation; this was done in the usual way. Pressures were recorded with a capacitance manometer and referred to a point 5 cm. below the sternal notch. Blood gases were analysed by the Van Slyke-Neill manometric method, and expired air in the Haldane apparatus.

15 women operated on between 1952 and 1955 while not pregnant became pregnant some time after the operation. All attended regularly throughout the pregnancy at the department of cardiology at the Royal Infirmary and were confined at St. Mary's Hospital, Manchester. Postpartum cardiological supervision has continued to the

present time. The remaining 12 women were operated on between the tenth and thirty-first weeks of pregnancy. They were followed up for at least six months after delivery. 26 of the women were operated on either at the Royal Infirmary by Mr. W. F. Nicholson or at Park Hospital by Mr. Gordon Jack or by Mr. John Dark; the remaining woman was operated on at Crumpsall Hospital by Mr. Herbert Haxton.

Valvotomy during Pregnancy (12 Cases)

Previous Pregnancies

5 of these patients had been previously pregnant, and 3 of these had passed through a single trouble-free pregnancy with eventual delivery of a living child. The intervals since these pregnancies were long; ten years (case 6), five years (case 2), and four years (case 10). In case 11 there had been two previous pregnancies one and two years previously; both pregnancies were complicated by severe incapacity with attacks of nocturnal dyspnœa, but both went to term. In case 4 three pregnancies had occurred eight, six, and four years previously; there were no cardiac symptoms before, during, or after the first pregnancy, but severe dyspnœa developed in both subsequent pregnancies, being worse in the third. Nevertheless all three pregnancies went to term.

Capacity for Effort before Current Pregnancy

1 patient was placed in group I (A.H.A. classification) 8 were placed in group II, and 3 in group III. By comparison with patients submitted to valvotomy apart from pregnancy these patients were less severely incapacitated before the pregnancy, but their incapacity increased during the pregnancy. The sizes of the mitral openings found at operation corresponded to this clinical difference, 7 of the 12 pregnant patients having mitral orifices estimated at 1 cm. or more in diameter, whereas this was so in only 7 of 15 non-pregnant patients.

Indications for Valvotomy

Mitral stenosis was the sole lesion in all the cases. In 8 the operation was undertaken because of attacks of nocturnal dyspnœa associated with clinical and radiological evidence of severe pulmonary congestion, and severe dyspnœa on effort. The 4 other patients had severe effort dyspnœa and pulmonary congestion but no nocturnal dyspnœa. 3 patients developed hæmoptysis for the first time during the pregnancy.

Results of Valvotomy

The operation was undertaken at various stages of pregnancy from the tenth to the thirty-first week. In 10 cases the final diameter of the valve was estimated as exceeding 3 cm.; in case 11 the split was regarded as poor and the diameter estimated as more than 2 cm. This patient remained dyspnœic on effort and orthopnœic and developed acute pulmonary œdema three days post partum. There were several postoperative complications in some of the 11 cases with satisfactory splits:

In case 4 a right hemiplegia developed six hours after the operation, but the cardiac symptoms were completely relieved, and the delivery was normal.

In case 12 fever, arthralgia, and a raised erythrocyte-sedimentation rate marked the onset of active rheumatism eight days after the operation. This was associated with the onset of auricular flutter and congestive heart-failure, which proved resistant to treatment, and abortion occurred thirty days after the operation; thereafter rapid improvement took place, with the restoration of sinus rhythm and the disappearance of heart-failure and signs of rheumatic activity. A year later the patient was entirely symptom-free (group I).

TABLE I—DATA OF TWELVE PATIENTS OPERATED ON WHILE PREGNANT

Case no.	Age (yr.)	Functional group before pregnancy	Parity	Valve size (cm.)		Mode of delivery	Functional group 6 mos. post partum	Remarks
				Before	After			
1	35	II	1	<1	3–4	N.F.T.	I	
2	27	II	2	1·3	2·5	N.F.T.	I	
3	22	III	1	<1	3	N.F.T.	I	
4	29	II	4	1	>3	N.F.T.	I	Right hemiplegia
5	31	III	1	<1	3	Abortion	—	Died 7 weeks after operation
6	28	II	2	0·5	4	N.F.T.	I	
7	22	III	1	0·75	3–4	N.F.T.	I	
8	20	II	1	1	3	N.F.T.	I	
9	27	I	1	2	3·5	N.F.T.	I	
10	23	II	2	1	4–5	N.F.T.	I	
11	23	II	3	<2	>2	N.F.T.	II	Pulm. œdema 3 days post partum
12	25	II	1	1	3·5	Abortion	I	Reactivated rheumatism

N.F.T., normal full term.

In case 5 operation was difficult, and this valve was eventually divided with a Bailey knife to give a diameter of about 3 cm. Two days after the operation a cerebral embolism occurred and heart-failure developed. Thirty-four days after the operation the patient was delivered of a stillborn fœtus, but heart-failure continued until death seven weeks after the operation.

Final assessment six months post partum showed that 10 of the 11 survivors were symptom-free (group I); the remaining patient was classified in group III.

These observations are summarised in table I.

Published Cases

77 cases reported in the Anglo-American literature are summarised in table II. There was only one maternal death, and there were three operatively induced abortions. Most workers consider the operative results to be good, and, with one exception, all the patients appear to have gone to term and been delivered normally. Including our 12 cases the total is 89 women operated on during pregnancy, with two deaths (2·2%), five abortions (5·6%), and eighty-four living children.

Pregnancy following Valvotomy (15 Cases, 16 Pregnancies)

Results of Pregnancy

There were no maternal deaths, but four children were lost in sixteen pregnancies. 10 of these patients had been pregnant before valvotomy, and their fifteen pregnancies had produced seven living children. Six of the eight losses were due to the cardiac condition. Of the four children

TABLE II—COLLECTED RESULTS OF MITRAL VALVOTOMY DURING PREGNANCY

Reference	No. of cases	Maternal deaths	Abortions	Remarks
Cooley and Chapman (1952)	1	0	0	..
Parkinson (1953)	1	0	0	..
Burwell and Ramsey (1953)	7	1	0	..
Cooley and DeBaky (1954)	5	0	0	..
Crawshaw et al. (1954)	12	0	0	..
Mulcahy (1954)	3	0	0	..
Watt et al. (1954)	7	0	0	4 still pregnant at time of writing
Sellors et al. (1955)	2	0	0	..
Glover et al. (1955)	5	0	1	..
Mendelson (1955)	10	0	0	..
O'Connell and Mulcahy (1955)	1	0	0	Full-term op.
Turner and Fraser (1956)	5	0	0	..
Marshall and Pantridge (1957)	18	0	2	..
Present series	12	1	2	..
Total	89	2 (2·2%)	2 (5·6%)	..

lost in the post-valvotomy pregnancies one was eight weeks premature and survived only twenty-four hours; one was stillborn owing to strangulation by the cord; one was lost after cæsarean section at thirty-eight weeks because of toxæmia; and in the remaining case therapeutic abortion was undertaken at fourteen weeks owing to the cardiac condition. Therefore only one child was lost owing to the cardiac condition. Thus, from the point of view of survival of mother and child, the post-valvotomy pregnancies gave good results.

Symptoms during Pregnancy

Despite these good overall results the pregnancies were by no means trouble-free:

3 patients (cases 16, 24, and 28) experienced orthopnœa and attacks of nocturnal dyspnœa beginning in the second trimester.

Case 23 had a severe hæmoptysis in the thirty-sixth week.

Cases 13 and 14 had attacks of frank pulmonary œdema in the eighteenth week (case 13) and three days post partum (case 14).

Case 27 went into congestive heart-failure in her fifteenth week and needed supportive treatment until term.

In 2 of these patients (cases 14 and 23) the operation had been regarded as satisfactory in every way. The 5 others were unsatisfactory either because of adverse features present before operation (auricular fibrillation and a considerably enlarged heart in cases 18 and 27 respectively) or because the final size of the valve was considered inadequate (cases 13, 16, and 24).

Time between Operation and Pregnancy

The time elapsing between the operation and the completion of the pregnancy varied from eleven months (case 22) to nearly four years (case 18).

There appear to be no grave disadvantages associated with becoming pregnant shortly after successful valvotomy, the 2 patients (cases 19 and 22) achieving it within three months both having an uneventful pregnancy and confinement.

Nor is a long interval between valvotomy and gestation necessarily disadvantageous, because case 22 underwent a second pregnancy uneventfully two years after the first. If the interval is long, a careful reassessment must be made to discover if there has been deterioration; this is exemplified by case 28. This patient, who appears in table I as case 3 because she was operated on during pregnancy, is of especial interest, and her case is therefore reported in full.

Case 3 (**28**).—A woman, aged 22, was seen in September, 1953, when she was eight weeks pregnant. She had been short of breath on exertion for two years, and six months previously had had an attack of acute dyspnœa characterised by the production of frothy pink sputum. Examination revealed pure "tight" mitral stenosis with radiological evidence of moderate pulmonary congestion and the electrocardiographic appearances of right ventricular hypertrophy.

Operation and Progress.—Mitral valvotomy was done on Oct. 7, 1953. The valve was estimated initially to be 0·7 cm. in diameter and was enlarged to more than 3·0 cm. Convalescence was uneventful. Biopsy of the auricular appendage showed "active rheumatism". The patient kept well during the remainder of the pregnancy and had a normal labour on May 14, 1954. When finally assessed in August, 1954, she admitted to no symptoms and was classified as group I, although neither radiography nor electrocardiography showed any appreciable improvement since before the operation. During the winter of 1955–56 she again noticed shortness of breath on effort but improved with the warmer weather.

Next pregnancy.—In January, 1957, she attended again when sixteen weeks pregnant; she had become much more short of breath and had had three nocturnal attacks of dyspnœa with frothy white sputum. On examination, in addition to the signs in the heart, there were crepitations at both lung bases. At cardiac catheterisation on March 1, 1957, the mean resting pulmonary arterial pressure was 61 mm. Hg, the pulmonary capillary venous pressure 31 mm. Hg, and the cardiac output 5·7 litres a minute. Medical management was adopted; the patient at present requires a good deal of rest and a restricted intake of salt.

It is difficult to know whether the valve has become stenosed again. Although the split was good both in the surgeon's estimate and, initially, in terms of function, objective evidence of improvement was lacking. Clearly, however, an apparently successful valvotomy followed by trouble-free pregnancy and confinement does not guarantee that subsequent pregnancies will be equally trouble-free. Had this patient not previously been operated on, the symptoms, the physical findings, and the results of catheterisation were such that operation would probably have been advised.

These data are summarised in tables III and IV.

Discussion

Despite the fears expressed by Burwell (1954) it seems that the complication of pregnancy does not add appreciably to the operative risk; the operative mortality of 2·2% approximates closely to the anticipated mortality in a group of patients in functional groups II and III. It

TABLE III—DATA OF PATIENTS BECOMING PREGNANT AFTER VALVOTOMY

Case no.	Age (yr.)	Cardiac rhythm	Time after operation (mos.)	Functional group		Valve size (cm.)		Complications during pregnancy	Mode of delivery
				Before	After	Before	After		
13	19	Sinus	24	III	II	Tight	N.A.	Pulm. œdema in 18th wk.	N.F.T.D.
14	22	Sinus	27	II	I	1	3	Pulm. œdema, 3 days post partum	N.F.T.D.
15	25	Auricular fibrillation	19	II	I	0·7	3	Nil	8 wk. premature (child died)
16	28	Sinus	16	III	II	N.A.	N.A.	Nocturnal dyspnœa and hæmoptysis	Full-time stillbirth (knotted cord)
17	35	Sinus	21	III	I	<1	3	Nil	N.F.T.D.
18	30	Auricular fibrillation	45	IV	II	0·5	2–3	—	Terminated in 14th wk., deteriorating
19	26	Sinus	12	III	I	<1	3	Nil	N.F.T.D.
20	29	Sinus	29	III	I	0·5	2·5–3	Nil	N.F.T.D.
21	20	Sinus	14	II	I	<1·5	2·5–3	Nil	N.F.T.D.
22	30	Sinus	11	III	I	1	4	Nil	N.F.T.D.
			35					Nil	N.F.T.D.
23	28	Sinus	29	II	I	1	3–4	Hæmoptysis in 36th wk.	Cæsarean section in 38th wk. (toxæmia) child died
24	32	Sinus	29	II	II	1·5	2·5	Nocturnal dyspnœa in 30th wk.	N.F.T.D.
25	25	Sinus	29	III	II	0·5	2·5	Nil	N.F.T.D.
26	35	Sinus	23	III	I	1	3	Nil	N.F.T.D.
27	31	Auricular fibrillation	22	III	II	1	3	Congestive heart-failure from 15th to 40th wk.	N.F.T.D.
*28	27	Sinus	36	III	I	0·7	3	Nocturnal dyspnœa 12th wk.	Still pregnant

* Case 3 in table I. N.A., not available. N.F.T.D., normal full-term delivery.

TABLE IV—COURSE AND RESULT OF PREGNANCY BEFORE AND AFTER VALVOTOMY IN TEN CASES

Case no.	Previous pregnancies		Date of operation	Subsequent pregnancies	
	Date	Mode of delivery and complications		Mode of delivery	Complications
15	1952 1954	Spontaneous abortion at 3 mos. Spontaneous abortion at 3 mos.	March 8, 1954	8 wk. prem.	Child survived 24 hr.
16	1947 1952	N.F.T.D. Therapeutic abortion	Feb. 11, 1954	N.F.T.D.	Stillbirth, knotted cord Nocturnal dyspnœa and hæmoptysis
17	1942	N.F.T.D.	March 8, 1954	N.F.T.D.	
18	1945	N.F.T.D., dyspnœa and hæmoptysis	April 24, 1952	Termin. in 14th wk.	Congestive heart-failure
20	1950 1952	Induced labour, dyspnœa Terminated in 14th wk. dyspnœa	May 4, 1953	N.F.T.D.	
21	1952	N.F.T.D., P.N.D. at 6 mos.	June 13, 1955	N.F.T.D.	Hæmoptysis in 36th wk.
22	1946 1949	N.F.T.D. N.F.T.D.	June 21, 1954	1955 N.F.T.D. 1957 N.F.T.D.	
25	1950 1952	N.F.T.D., pulm. œdema 3 days post partum Terminated in 12th wk. dyspnœa	April 29, 1953	N.F.T.D.	
26	1943	N.F.T.D.	Nov. 4, 1954	N.F.T.D.	
27	1953	Terminated in 22nd wk. dyspnœa	May 2, 1955	N.F.T.D.	

N.F.T.D., normal full-term delivery. S.B., stillborn. P.N.D., paroxysmal nocturnal dyspnœa.

is difficult to contrast these results with those obtained by medical management, because data from comparable series of cases are not available.

Morgan Jones (1952) found the maternal mortality due to heart-disease in 543 cases in which there was no definite cardiac contraindication to pregnancy to be 0·7%. In 343 of these cases, in which there were symptoms and some pulmonary congestion, the mortality was 1·1%. The maternal mortality is probably increased by valvotomy during pregnancy by contrast with medical management, but this increased risk is certainly not more than that which would be incurred if the pregnancy was allowed to continue without operation and valvotomy was done post partum. Correct perspective therefore demands taking into account how many patients would ultimately come to operation and whether pregnancy merely brings forward the time at which the operation is done.

It has been observed previously (Marshall and Pantridge 1957) that the added burden of pregnancy may cause a moderately stenosed valve (1·5–2·0 cm. in diameter) to simulate tight stenosis in the non-pregnant state; but, irrespective of the pregnancy, operation was merited on the basis of the symptoms and signs and the size of the valve in 8 of our 12 pregnant patients. It must be admitted that, had they not become pregnant, operation would not have been advised because of the symptoms in the remaining 4, and it is difficult to say whether it would ultimately have been required.

These women with only moderate stenosis could have been managed medically, but the possibility of future pregnancies, the uncertain prognosis, and the fact that 3 of our 4 such patients were functionally improved when their postpartum state was compared with their condition before pregnancy all argue in favour of operation.

Surgery does not appear dangerous to the fœtus. The fœtal mortality of 5·6% (table II) compares favourably with that of 8·6% cited by Hamilton (1947) and 10·2% in 990 pregnancies complicating all forms of heart-disease seen in this department in 1946–51, more than half of them (6·4%) being terminated because of the heart-disease (unpublished data). The anticipated abortion-rate in healthy women from the twelfth week of pregnancy onwards is about 2% (Eastman 1955).

We therefore feel that, if during pregnancy the symptoms are severe enough to warrant it and the valve is technically suitable, valvotomy is the treatment of choice. Even in cases seen within the first few weeks of pregnancy we doubt if Burwell and Metcalf (1954) are correct in regarding termination as the safest course. In favour of termination is the fact that, if valvotomy is attempted and fails, the pregnancy may by then have progressed so far that there is no longer any alternative to going on to term. This is a valid criticism, but it must be remembered that termination is not entirely safe, and 2 of the deaths due to heart-disease in Morgan Jones' (1951) series of 352 cases followed termination. Our experience does not suggest a preferential time for surgery. It seems reasonable to operate sufficiently early for convalescence to remain uncomplicated by premature labour, but the patient of O'Connell and Mulcahy (1955) was operated on at term with good results.

Our findings emphasise that patients who have had a good operation both in terms of increased size of the valve and subsequent functional improvement may nevertheless encounter difficulties during pregnancy. 10 of our patients were considered excellent results in every way; yet 1 had pulmonary œdema three days post partum, and 1 other had attacks of nocturnal dyspnœa as early as the twelfth week. Glover et al. (1955) also report a case in which, after an apparently successful valvotomy, pregnancy was complicated by postpartum pulmonary œdema; but Harken (1953) reported fifteen uncomplicated pregnancies and confinements following operation.

These paradoxical observations again reflect the fact that, whereas pregnancy may cause moderate stenosis to simulate tight stenosis, the operative conversion of tight to moderate stenosis may be sufficient to give a good functional result in a non-pregnant woman.

The work of Donald et al. (1957) suggests that a considerable degree of narrowing of the valve may persist after operation, because in 8 of 9 patients classified as excellent results, the resting pulmonary capillary venous pressure was 20 mm. Hg or higher. Since the cardiac output was subnormal in most of these patients, it can be appreciated that the increased cardiac output of pregnancy may cause a considerable increase in pulmonary capillary venous pressure. In 2 of their "excellent" cases Donald et al. found that raising the output by 75% by exercise increased the pulmonary capillary venous pressure from 23 to 57 mm. Hg and from 28 to 49 mm. Hg. In 5 of our 6 cases in which the operative results were less than excellent severe symptoms were encountered during pregnancy. It therefore appears that, although a woman who has undergone a successful operation and subsequently is placed in group I will usually go through pregnancy without trouble, this is not necessarily the case, and difficulties are to be expected in those with less successful operative results.

In women operated on before conception the intervals between operation and confinement varied from eleven

to forty-five months, and there is no evidence that any particular interval is to be preferred. It seems reasonable to delay conception until an accurate postoperative assessment can be made, and this probably cannot be made in less than six months. After this there are strong arguments for encouraging early conception, because probably in a proportion of patients a good result may not be lasting (Baker et al. 1955). There is therefore a greater need for careful assessment if the interval after operation is long. This tendency to deterioration may partly explain the relative absence of trouble in patients operated on during pregnancy by contrast with those in whom the operation antedated pregancy, but (as already noted) the two groups are not comparable as regards the severity of the disease.

Summary and Conclusions

The results in 12 patients with mitral stenosis submitted to mitral valvotomy while pregnant are reported, together with those in 77 published cases.

In these 89 cases the operative mortality was 2·2% and the abortion-rate 5·6%.

It is concluded that : (1) pregnancy does not appear to increase the operative risk; (2) by contrast with medical management the operation does not increase the fœtal mortality ; and (3) in suitable cases valvotomy seems preferable to termination.

Seventeen pregnancies in 16 patients who had previously undergone mitral valvotomy are reported: twelve living children were obtained by normal full-term delivery; one pregnancy was terminated at fourteen weeks because of heart-failure; 1 patient was delivered by cæsarean section at thirty-eight weeks because of toxæmia; there were two fœtal deaths unrelated to the mothers' heart condition; and 1 patient is still pregnant.

Symptoms due to severe pulmonary congestion were encountered in 3 of 10 patients placed in function group I after the operation and in 5 of 6 patients placed in group II.

It is concluded that: (1) although pregnancy following successful valvotomy is usually safe, difficulties may be encountered; (2) a technically unsatisfactory operation, even if followed by reasonable functional improvement, is unlikely to permit of a trouble-free pregnancy; and (3) assessment of fitness for pregnancy cannot be satisfactorily undertaken sooner than six months after the operation. Delay in conception after this may be disadvantageous.

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POTASSIUM DEFICIENCY IN LIVER DISEASE
CAUSING MUSCULAR WEAKNESS AND POLYURIA

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Low serum-potassium levels in patients with liver disease have been reported several times in recent years, but without any clinical consequence beyond changes in the electrocardiogram.

Severe potassium-deficiency in the two patients with cirrhosis of the liver described here caused muscular weakness and nephropathy. The potassium deficiency was attributed to excessive loss of potassium in the urine; the cause and significance of such loss are discussed.

Case-reports

FIRST CASE

A married woman, aged 30, was admitted to the Derbyshire Royal Infirmary on June 25, 1954. She was very ill on admission. The history was of fatigue since the birth of her second child a year previously; jaundice for 10 weeks; weakness of her limbs for 6 weeks, which made it necessary for her to use a stick in the house and impossible for her to do her housework, and which caused her to fall frequently; thirst and frequency of micturition for six weeks; and amenorrhœa for two months.

The prominent signs were extreme air-hunger, jaundice, enlargement of the liver and spleen, increased pigmentation, spider nævi, and great weakness. She could not sit without support, and her voice trailed away into silence when trying to answer questions. The patellar reflexes were not obtainable and the tendo-achillis reflexes were very weak.

Investigation and Treatment

The alkali reserve was 10·8 mEq. per litre of plasma, the serum-sodium 130 mEq., the plasma-chloride 98 mEq., the serum-potassium 1·7 mEq., the blood-urea 48 mg. per 100 ml., and the serum-bilirubin 3·7 mg.%; the other liver-function tests were grossly deranged. The urine pH was 7·1 on the day of admission, and 7·3 and 7·4 on the second and third days of treatment. There were between 15 and 20 pus cells in the urine in each high-power field. The electrocardiogram (E.C.G.) showed evidence of potassium depletion (fig. 1).

The alkali reserve was restored in 2 days by intensive oral sodium-bicarbonate therapy, but it was 24 days before the serum-potassium reached 3·4 mEq. per litre with a daily dose of 16 g. of potassium chloride (214 mEq.) for the first week; by this time all reflexes had returned, and doses of 8 g. daily

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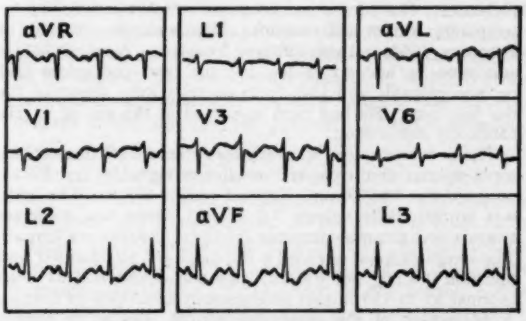

Fig. 1—Case 1 : electrocardiogram on admission.

(107 mEq.) were given thereafter. The electrocardiographic changes improved slowly and were closely correlated with the rising serum-potassium level, becoming normal after 25 days' treatment. The blood-urea fell to normal levels (23–30 mg. per 100 ml.) after 10 days of therapy. Jaundice disappeared; the serum-bilirubin fell to normal levels but the other liver-function tests remained grossly deranged. There was no tetany and the lowest level of serum-calcium was 8·6 mg. per 100 ml. on the day of admission.

The specific gravity (S.G.) of the urine throughout the 24 hours varied only between 1008 and 1010; it was still 1010 after 12 hours without fluid, and dropped only to 1006 after a litre of fluid. The daily sodium output in the urine was 170 mEq., and the potassium output was 46 mEq. on the 6th day, 39 mEq. on the 7th day, and 79 mEq. on the 26th day, when the oral supplements of potassium chloride were 214 mEq., 214 mEq., and 107 mEq. respectively. On the 4th and 5th days the CO_2 content of the urine was 8·7 mEq. and 6·5 mEq. per litre when the oral dose of sodium bicarbonate was 12 g. (143 mEq.) daily. Chromatography of the urine (Prof. C. E. Dent) showed no excess of aminoacids.

Subsequent Course

She was discharged after 4 weeks, taking as maintenance therapy potassium chloride 8 g. and sodium bicarbonate 16 g. daily. She remained well and was readmitted 6 weeks later for investigation. The liver-function tests were still abnormal, but the pus cells had disappeared from the urine and the ability to concentrate the urine was restored; the S.G. after a 12-hour fluid-fast was 1020 and the S.G. on dilution 1006. Alkalinisation by acetazolamide (250 mg.) increased the urine pH from 7·1 to 7·8, and acidification by ammonium chloride (5 g.) decreased the pH from 7·1 to 6·3. The daily urinary output averaged just over 4 litres.

She remained well on the same maintenance therapy, and was readmitted for investigation 15 months later. Treatment by sodium bicarbonate and potassium chloride was stopped for 2 weeks. In this time the alkali reserve fell from 24 mEq. to 14 mEq. per litre, the serum-potassium from 4·0 mEq. to 3·4 mEq. per litre, and the urinary potassium from 96 mEq. to 28 mEq. in 24 hours. Treatment was recommenced before an operation for the removal of a rectal polyp which was causing some rectal hæmorrhage. Bleeding was severe after the operation and hepatic failure supervened. She was restored by treatment and discharged herself 2 weeks later.

5 days later she was readmitted in hepatic failure and died. At necropsy there was multilobular cirrhosis of the liver. There was no tumour in the adrenal cortex. Mild chronic pyelonephritis was present, with focal tubular calcification. A specimen of urine was sent to Dr. A. H. Gowenlock, 10 days before death; he reported that it contained 20·5 μg. of aldosterone in 24 hours (normal 4·6 to 23·5 μg). She was excreting 119 mEq. of potassium daily at the time of the estimation, and was taking 8 g. daily of potassium chloride (107 mEq.).

SECOND CASE

A man, aged 49, was first admitted to St. Bartholomew's Hospital in May, 1954. He had been in another hospital in November, 1953, for a hæmatemesis, which was followed by temporary ascites and œdema. Hæmatemesis recurred in February, 1954, and was followed by ascites. A month before admission he had no ascites, but the liver and spleen had become palpable and liver-function tests were abnormal for the first time. He had been jaundiced at the age of 7. He habitually drank stout.

The liver and spleen were enlarged; there were three spider nævi, palmar erythema, and small hæmorrhoids; the blood-pressure was 130/70 mm. Hg, and weight 155 lb. The urine was normal (daily volume 1·5 litres). There was moderate anæmia and thrombocytopenia (platelets 115,000 per c.mm.). The serum-proteins were 7·8 g. (albumin 4·8, globulin 3·0) and bilirubin 0·5 mg. per 100 ml.; pseudocholinesterase 51 units (normal 55 to 125 units); prothrombin level 33% of normal. A radiograph of the chest was normal; swallowed barium showed small varices at the lower end of the œsophagus; on excretion urography anatomy and function were normal.

At operation (Mr. A. H. Hunt) the liver appeared cirrhotic. After biopsy, the portal vein was anastomosed to the inferior vena cava. Recovery was uneventful. The liver biopsy showed portal cirrhosis.

During the next 6 months the spleen became impalpable. For a further year he remained well, though thrombocytopenia persisted (platelets about 70,000 per c.mm.), his liver enlarged, and his weight gradually increased. In March, 1956, he was weak and breathless on exertion, with hepatic fœtor and ankle œdema.

Second Admission

He was readmitted on May 10, 1956. Polyuria and thirst had been noticed for several weeks. He was euphoric and confused, with a fine tremor of the fingers. There was œdema to the waist and moderate ascites; weight 178 lb. Secondary sexual hair was sparse, the skin was brown, and there was slight jaundice. The pulse was collapsing, and the blood-pressure 180/45 mm. Hg; a harsh systolic murmur was loudest at the apex; there were moist sounds at the left lung base. The firm, rounded liver-edge was 3 cm. below the costal margin. He drank 4 to 6 litres of fluid daily and passed much dilute urine (S.G. 1004–1005). Chest radiography showed pulmonary vascular engorgement, enlargement of the heart, and small bilateral pleural effusions. The E.C.G. showed widespread abnormalities of the ST segments and T waves. There was a mild anæmia; the platelet count had risen to normal. Serum-

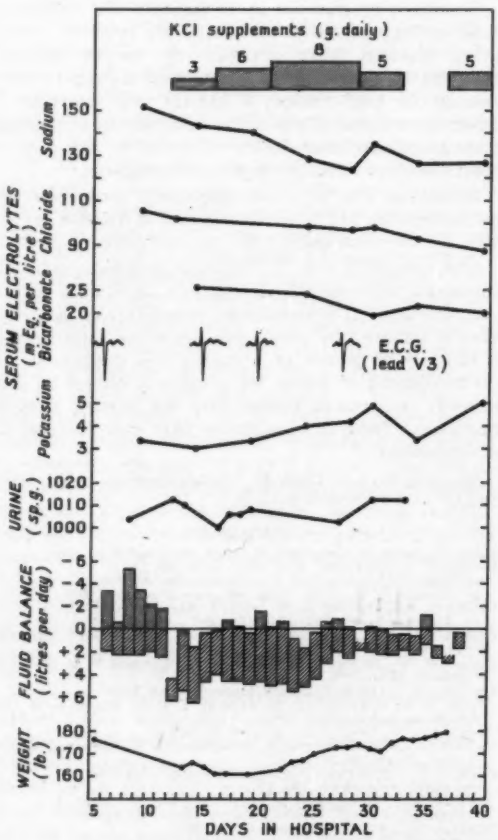

Fig. 2—Case 2: potassium supplements, serum electrolytes, E.C.G., S.G. of urine, fluid-balance, and body-weight during last admission. Fluid intake is plotted downwards from the zero line, and urine output upwards. Collection incomplete on days 29 and 37.

proteins were 5·8 g. per 100 ml. (albumin 2·6, globulin 3·2) and bilirubin 5·7 mg. per 100 ml.; pseudocholinesterase 35 units; prothrombin level 18% of normal; alkaline phosphatase 27·5 King-Armstrong units. The blood-urea was 19 mg. per 100 ml.

On May 14 (day 5 of fig. 2) he became drowsy, and was given oral chlortetracycline and sodium glutamate (23 g. daily). On a fluid intake of 2 litres daily he continued to pass large quantities of dilute urine (fig. 2). His weight, œdema, jaundice, and drowsiness diminished. Serum electrolytes on day 9 were sodium 152, potassium 3·3, and chloride 105 mEq. per litre.

Stupor developed on day 12, with flapping tremor, increased tendon-jerks and fœtor. Protein was withheld and large doses of glucose were given by mouth. There was heavy glycosuria, and the blood sugar was 460 mg. per 100 ml. Instead of sodium glutamate, glutamic acid was given (20 g. daily), and oral potassium chloride was started (3 g. daily).

In the next 2 days he improved to his original state of mild confusion, but flapping tremor persisted. Ascites was absent on day 14, and the liver smaller. The blood-sugar was 128 mg. per 100 ml., and glycosuria ceased. Serum-electrolytes were sodium 143 mEq., potassium 2·9 mEq., bicarbonate 25·7 mEq. per litre, calcium 9·6 mg. per 100 ml. The E.C.G. showed further ST-segment changes and prominent U waves, as in hypokalæmia (Bellet 1955). He was allowed 20 g. of protein daily, 200 g. of carbohydrate, and 500 mg. of salt.

The daily dose of potassium chloride was increased to 6 g. on day 16, and to 8 g. on day 21, but the serum-potassium rose only slowly, and improvement of the E.C.G. was no more rapid (fig. 2). Polyuria and polydipsia continued. Fluid deprivation was tolerated for only 6 hours on day 18; the minimum urine-flow was 3 ml. a minute, and the maximum S.G. was 1006. Next day he was given 10 units of vasopressin ('Pitressin') subcutaneously, and was allowed to drink 400 ml. per hour. In the first hour the urine S.G. reached 1008. The rate of urine-flow fell from 5 to a minimum of 3·3 ml. per minute (during the 2nd hour).

During day 22, when his intake of sodium was 9 mEq., and his dietary potassium being supplemented by 107 mEq. of potassium chloride, the urine contained 70 mEq. of sodium, 97 mEq. of potassium, and 18·9 g. of urea in 5·4 litres—suggesting potassium retention accompanied by sodium loss, as in the repair of a potassium deficit. The daily urinary output of calcium was 342 mg. An oral glucose-tolerance test on day 21 gave a high normal curve. Urea clearance was normal on day 24. Radiography of the pituitary fossa showed a small area of vascular calcification superimposed on the sella in the lateral view, but no other abnormality.

During the 4th week his weight increased again, with increasing œdema, but without ascites. The liver ceased to be palpable. Clinical signs of an overactive circulation were supported by measurement of blood-flow through the feet, which was about four times the normal (Dr. R. S. Duff). Fluoroscopy showed a large left ventricle and exaggerated pulsation of the pulmonary vessels. The blood-pressure had fallen gradually to 115/40 mm. Hg.

At the end of the 4th week the E.C.G. was less abnormal, the serum-potassium was up to 4·2 mEq., and the serum-sodium down to 124 mEq. per litre. Excretion urography showed only faint dye shadows, but normal anatomy. The daily output of urine declined to about 2 litres, and thirst ceased. The serum-potassium level rose to 4·9 mEq. per litre on day 30; potassium chloride was omitted for 6 days, but given again after the serum-potassium was found to have fallen to 3·3 mEq. per litre. The low serum-sodium was not appreciably influenced by substitution of sodium glutamate for glutamic acid, increasing the daily intake of sodium to 36 mEq. on day 28 and to 108 mEq. on day 37.

On day 34 the serum-proteins were 4·6 g. per 100 ml. (albumin 1·7, globulin 2·9), and œdema was generalised. The area of liver dullness disappeared. Epistaxes, increasing stupor, and ankle clonus heralded the coma in which he died on the 40th day. Permission for necropsy was refused.

Discussion

The severe muscular weakness of the first patient was due to potassium deficiency, which also caused characteristic electrocardiographic changes. Both responded gradually to potassium supplements while the serum-potassium level rose slowly to normal. Her urine was of low and almost constant specific gravity, with a high pH and bicarbonate concentration which, taken with the low serum-bicarbonate concentration, was indicative of defective tubular reabsorption of water and bicarbonate. There was a minor degree of nitrogen retention and of pyuria, and there was some histological evidence of pyelonephritis at necropsy. The renal function improved considerably with potassium repletion. Moreover, she had symptoms of potassium deficit before those of renal damage. The findings can well be explained as due to the nephropathy of potassium depletion (Relman and Schwartz 1956) with a pyelonephritis superimposed (Eales and Linder 1956). Calcification has been noted in the renal tubules of potassium-deficient animals (Follis et al. 1942); but Fourman and McCance (1955) implied that renal calcification in their patient was the natural result of the increased calcium excretion of acidosis.

The renal loss of bicarbonate was presumably the cause of the acidosis, and this would sufficiently explain the absence of the alkalosis which is expected in potassium deficiency. "Renal tubular acidosis" is characterised by potassium loss, but in this condition the administration of an adequate amount of sodium bicarbonate is usually enough to prevent loss of potassium. The plasma-chloride was never raised in case 1.

The second patient had a vasopressin-resistant diabetes insipidus which diminished as the serum-potassium and the E.C.G. gradually returned towards normal on large potassium supplements. Glycosuria on days 12 and 13 raised the S.G. of the urine to 1012 and 1010, as happens with an osmotic load in classical diabetes insipidus (Brodsky and Rapoport 1951); otherwise the S.G. did not exceed 1008 in the first 4 weeks. Hyposthenuria unresponsive to vasopressin is a recognised feature of the nephropathy of potassium depletion (Relman and Schwartz 1956). It is also seen as a familial condition, and rarely in a variety of renal disorders which are unlikely to have been present in this patient. There may have been some "renal tubular acidosis", since the serum-bicarbonate level was not raised; but a low serum bicarbonate level in early hepatic coma may also be due to hyperventilation (Vanamee et al. 1956).

Neither patient had frank or latent tetany; its relation to potassium deficiency and acid-base balance is still obscure (Fourman and McCance 1955).

We conclude that there was severe potassium deficiency in both cases, causing paralysis and probably nephropathy in the first, and vasopressin-resistant diabetes insipidus in the second. Repletion with potassium, which required continued administration of large doses, was of great benefit in the first case and probably useful in the second.

Cause of the Potassium Deficiency

There was no reason to suspect deficient potassium intake in either patient, and neither had chronic diarrhœa to suggest loss from the gut. So renal loss is most likely. Mahler and Stanbury (1956) collected figures for the renal potassium output of normal people at various serum-potassium levels; by this standard all the output figures for our patients are excessive, except the last in case 1, which is high normal.

Urinary excretion of potassium is excessive in some cases of primary renal disease. Since potassium deficiency causes renal disorder, the distinction can be difficult. The history of case 1 and her improvement on potassium supplements suggest that pyelonephritis was a consequence of potassium deficiency rather than its cause. In case 2, the absence of other signs indicates that the renal disorder was solely due to potassium deficiency. Renal loss of potassium can be caused by mercurial diuretics and by acetazolamide, but neither was given. It can also be induced by heavy osmotic loads of some sodium salts (Rapoport et al. 1949). Sodium glutamate may have had an effect of this kind in case 2, but it is unlikely to have been important.

Aldosterone causes renal loss of potassium, especially in patients with primary aldosteronism (Conn 1955). Case 1 did not have an adrenal tumour, her urinary excretion of aldosterone was only high normal, and none of the other features of primary aldosteronism was present. Case 2 had a high serum-sodium level only during restriction of fluid intake, and impaired glucose tolerance; this may be seen in primary aldosteronism (Hewlett et al. 1957), but here may have been due to liver damage. Neither had definite hypertension: patients with cirrhosis of the liver, who have peripheral vasodilatation and a high cardiac output (Kowalski et al. 1954), rarely have hypertension, and may lose it (Loyke 1955).

The interactions of steroid hormones on electrolyte balance are still as uncertain as are the effects of liver disease on steroid hormone metabolism (Cameron 1957). But aldosterone is the steroid most likely to cause electrolyte effects like those of deoxycortone acetate (D.C.A.). Repeated large doses of D.C.A. can cause a condition in dogs very like primary aldosteronism in man (Kuhlmann et al. 1939, Ragan et al. 1940). A man has developed polyuria, polydipsia, paralysis, tetany, and E.C.G. changes, all probably due to potassium deficiency, after a large dose of D.C.A. (Moehlig and Jaffe 1942). The patients of Luft and Sjögren (1953), given D.C.A. for many weeks, had a steadily rising urinary output of calcium, while case 2 had a high urinary calcium output (which may have contributed to his polyuria) without a high serum-calcium level.

The urinary output of aldosterone is usually high in patients with œdema or ascites from cirrhosis of the liver, and is correlated with renal retention of sodium (Wolff et al. 1956). In this, as in other forms of secondary aldosteronism (Conn 1956), sodium retention is the dominant electrolyte effect. But potassium loss is a known hazard of congestive heart-failure and of the nephrotic syndrome; it may be more common in cirrhosis than is usually thought. Renal potassium loss due to aldosterone is likely to depend on the level of sodium intake (Relman and Schwartz 1957), and an unrecognised high salt intake could have been a factor in the development of potassium deficiency in our patients.

The need for potassium in the treatment of severe acute liver disease was pointed out by Latner (1950); the treatment of hepatic coma includes supplementary potassium (Sherlock et al. 1956). Low serum-potassium levels in a variety of more chronic liver disorders, especially cirrhosis, were reported by Wang (1952), and were common in patients with cirrhosis and œdema (Amatuzio et al. 1952). Patients with cirrhosis, even without œdema or ascites, had a low exchangeable potassium (Aikawa et al. 1953). Negative potassium balance due to renal loss has been reported in a few patients with liver disease (Fongi et al. 1954). Electrocardiographic change is the only consequence attributed to potassium deficiency in these reports. But in our patients the effects of potassium deficiency were so severe as to suggest that it is a complication of liver disease worth search and treatment—especially because the nephropathy of potassium depletion is reversible in its early stages (Relman and Schwartz 1956).

The paradoxical conjunction of œdema due to cirrhosis with diabetes insipidus (whether responding to vasopressin or not) has not been recorded before. Classical diabetes insipidus can exist with œdema of the " secondary aldosteronism " type, as in the nephrotic syndrome (Landau and Wajsman 1934). Vasopressin-resistant diabetes insipidus with œdema has been reported by White (1954) in a patient with cerebral metastases. A lesion of the tuber cinereum was thought by Biggart (1937) to be the cause of the development of resistance to vasopressin in a patient with diabetes insipidus; evidence is now accumulating that the secretion of aldosterone may be controlled by the hypothalamus (*Lancet* 1957). There was probably no lesion of the pituitary or hypothalamus in case 2.

Summary

Two patients with chronic liver disease were found to have severe potassium deficiency.

A woman, aged 30, presented with jaundice, muscular weakness, and polyuria. She had hypokalæmia with electrocardiographic changes and renal functional defects like those of potassium deficiency, and severe acidosis. The acidosis was of renal tubular origin, and was rapidly corrected by sodium bicarbonate. Large potassium supplements gradually corrected the other abnormalities, but signs of liver damage persisted, and she died 2 years later of hepatic failure. Necropsy showed multilobular cirrhosis and a mild chronic pyelonephritis.

A man, aged 49, had a portacaval anastomosis for recurrent hæmatemesis due to portal cirrhosis. His liver function gradually deteriorated during the next two years, until he was admitted with œdema and a diabetes insipidus resistant to vasopressin; he had hypokalæmia and corresponding electrocardiographic changes. Potassium repletion restored his ability to concentrate the urine before he died of hepatic failure.

The potassium deficiency is attributed to renal loss of potassium in both cases, and the possible causes of such loss are discussed, with particular reference to aldosterone.

We are grateful to Prof. C. E. Dent and Dr. A. H. Gowenlock for their special investigations of the urine in case 1; to Dr. G. W. Hayward and Mr. A. H. Hunt for permission to report case 2; and to Dr. R. S. Duff for measuring peripheral blood-flow.

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PILONIDAL SINUS OF THE UMBILICUS

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PILONIDAL sinus is of perennial interest particularly because of its sites and the theories about its ætiology. The case reported here provides yet another link in the important chain of evidence that pilonidal sinuses are unlikely to be congenital.

Soon after the first descriptions of pilonidal sinus in the usual sacrococcygeal position by Anderson (1847) that involving the umbilicus was noted by Warren (1854). Patey and Scarff (1946) reported and discussed the first of a collection of cases of pilonidal sinus in the hands and fingers of hairdressers, and in so doing caused a complete swing in the tenets of ætiology of all pilonidal sinuses, away from the theories of developmental causes towards those observations showing acquired mechanical and secondary infective origins, the hairs being " sucked " into the skin, especially wherever there is a cleft or a web between parts of the body. Thus pilonidal sinus has been seen in the interdigital webs of the toes (Brearley 1955), in the axilla (Aird 1952), and in the perineum (Smith 1948, Edwards and Riemann 1950).

Patey and Williams (1956) described a pilonidal sinus of the umbilicus. They showed that there was a uniform,

The bundle of hairs, uniformly oriented, coming out of the umbilicus with a secondary opening above. The skin around has been shaved.

and not haphazard, orientation of hairs in the sinus, the roots being directed always towards the lining of the cavity. This seems to be a constant feature of pilonidal sinuses (Weale 1955), and it might reasonably be supposed that such an orientation of the roots should favour the theories that hold that such sinuses are developmental abnormalities, a haphazard arrangement favouring the " acquired " theory. However, Patey and Williams feel that, because the lesion of the umbilicus is most likely to be an acquired lesion, the uniform orientation shown cannot be the determining indication that the lesion is of congenital origin. Patey and Scarff (1955) suggest that all loose hairs will, even if sucked in, be propelled root first into the skin by reason of the direction of overlap of their scales.

In the present case there is a uniform orientation of hairs (see figure), which entered the skin via the umbilicus, there being a secondary opening above.

Case-report

An obese dark-skinned man, aged 56, moderately hirsute, was admitted for cholecystectomy. Examination of his abdomen revealed a bundle of hairs presenting at the umbilicus, coming out of a short track $^1/_4$ inch long. There had been no discharge or pain. The patient had not noticed it before; there was no history of the lesion in the days of adolescence or early adult life before he became so hirsute. Before his operation the hairs were removed quite easily. The sinus was not excised.

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EXTRAPERITONEAL COLOSTOMY

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LATERAL-SPACE obstruction is a well-recognised complication of left iliac colostomy. Closure of the lateral space can be technically quite difficult, and may not altogether preclude possibilities of strangulation of small bowel. Whether the space is closed from above or from below, loops of bowel can still be caught in the sulcus which is formed. Some surgeons resort to a midline colostomy, with a lateral space so large that strangulation is unlikely.

The similar risk of intestinal obstruction being caused when a drainage tube is passed obliquely into the peritoneal cavity (after anterior resection or some similar procedure in the pelvis) is circumvented by bringing the tube out extraperitoneally through a lateral stab wound. I have therefore applied this technique to the fashioning of a terminal colostomy following an abdomino-perineal operation. The descending colon, being still fixed in the lateral sulcus, is brought out extraperitoneally before passing through the other layers of the abdominal wall.

The fashioning of these colostomies is technically easier if it is done before the closure of the new peritoneal floor. Hæmostats are fixed to the edge of the peritoneum and the rectus sheath on the left-hand side of the wound. The skin is gently held with the same tension. A circle of skin about an inch in diameter is excised * at the normal site, together with a small

* A simple wad-punch purchased from a gunsmith and honed to a fine edge makes an excellent circular knife for cutting the skin and deeper tissues. The diameter should be one inch for colostomy and seven-eighths of an inch for ileostomy. If the skin is unusually tough the edge of the wad-punch may be supported gently by a block of wood held within the abdomen while the punch is struck gently with a mallet.

DR. HUBBLE: REFERENCES—*continued*

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amount of fat and aponeurosis of the external oblique. The internal oblique and transversus muscle are split in the line of their fibres, but care is taken *not* to pass through the peritoneum. With the finger a track is burrowed around the outside of the peritoneum to the raw surface posteriorly where the descending colon is taking attachment. Along this track the terminal bowel, previously crushed and divided, is guided by means of a large pair of Duval's forceps. The peritoneal floor is then closed in the usual way, and the colostomy is sutured to the skin margin with interrupted cotton sutures, as suggested by Hermon Taylor and described by Butler.[1]

Care should be taken that there is no kinking of any residual mobile sigmoid, between the lower end of the descending colon and the point where it begins to tunnel away beneath the peritoneum. If there is a tendency to kinking, it is well to pull more of the sigmoid through until the descending colon lies comfortably. Occasionally a number of interrupted sutures may be required just where the descending colon tunnels a way in its new extraperitoneal course.

Of late I have used the same method for creating a terminal ileostomy. In this operation, the lie of the mesentery may call for a little ingenuity.

I have found this procedure much easier than attempts to close the lateral space in the manner usually practised.

Preliminary Communication

MAMMOTROPHIC HORMONE IN SERUM OF HEALTHY WOMEN

THE urine of healthy women contains a hormone which induces a specific growth response in the rudimentary mammary glands of weanling male mice.[2 3] This hormone is probably not an œstrogenic steroid, and the results of a series of experiments in which female urine was injected into hypophysectomised weanling males suggest that it is produced by the anterior pituitary[4].

In this communication experiments are recorded in which the blood-serum of five normal premenopausal women, together with œstrone and progesterone, was injected into totally hypophysectomised weanling male mice. The results leave little doubt that a mammotrophic agent is present in recognisable amounts in the serum of healthy women, and afford further evidence that it is produced by the anterior pituitary.

METHODS

Totally hypophysectomised weanling male mice, of the reactive Strong A_2G strain, bred under strict supervision in our own laboratories, were used in all experiments. The sella turcica of each animal was serially sectioned at the end of each experiment. Each sella yielded approximately 250 sections. If anterior pituitary remnants were discovered the animal was discarded. In approximately one animal in five hypophysectomy proved to have been incomplete. Each animal was given, by subcutaneous injection, 0·1 ml. of human premenopausal serum, together with 0·125 μg. of œstrone and 0·75 mg. of progesterone twice daily for five days.

The mammary growth response was estimated by counting the number of large, deeply-staining, club-shaped swellings (" clubs ") at the duct ends of the mammæ and calculating the mean number of clubs per gland. No structure having a diameter less than twice that of its parent duct was counted as a club. It has previously been shown [5] that the presence in significant numbers of cellular clubs of this size in the mammæ of weanling males of the Strong A_2G strain is a clear indication of a growth response induced by an artificial and specific exogenous mammary stimulus.

During the past eighteen months, including the period covered by the experiments reported here, the mean number of large clubs per gland in the mammæ of untreated, intact weanling male mice of the age and strain used in these experiments has been estimated at regular intervals. This figure has been invariably less than 1·0, and over an adequate recent period has shown a range of 0·75 to 0·05 with a mean of 0·5.

RESULTS AND DISCUSSION

The accompanying table shows the intensity of the mammary growth response induced by the serum obtained from five healthy premenopausal women in the second half of the menstrual cycle.

RESPONSE OF HYPOPHYSECTOMISED MICE TO SERUM OF FIVE HEALTHY PREMENOPAUSAL WOMEN

Serum no.	Total no. of hypophysectomised mice	Total no. of mammary glands examined	Total no. of clubs	Mammary growth response (clubs per gland*)
1	6	34	123	3·5
2	11	65	128	2·0
3	10	59	365	6·2
4	9	53	213	4·0
5	10	58	267	4·6

* Untreated intact controls have 0·5 clubs per gland.

There is convincing experimental evidence that the administration of an œstrogenic steroid and progesterone to the hypophysectomised small mammal is powerless to induce a significant mammary growth response, providing that the hypophysectomy is proved to be complete by serially sectioning the sella.[6] We have previously shown this to be true of hypophysectomised Strong A_2G weanling male mice, and this experiment was repeated with negative results during the time the work now reported was in progress. A similar negative result was obtained when totally hypophysectomised weanling males were given prolactin alone over a period of five days.

On the other hand, we have been impressed by the vigour of the mammary reactions observed in animals of these control groups in which a relatively small and insignificant fragment of anterior pituitary was left behind, more especially if the fragment contained cells whose cytoplasm was eosinophilic.

Prolactin + œstrogen + progesterone invariably induces a mammary growth response in the totally hypophysectomised small mammal, and at optimal dose levels in reactive A_2G male weanlings this response is often spectacular. To eliminate the possibility in the experiments reported that the mice injected with human serum were in a non-reactive phase, we have controlled each experiment in which human serum + œstrone + progesterone were given by setting up, at the same time, a group of totally hypophysectomised weanlings which were given prolactin + œstrone + progesterone. A satisfactory mammary growth response was induced in all such controls and a similar but less intense response was obtained in all animals when human female serum was substituted for the prolactin of this hormone combination.

The quantitative extraction of the mammotrophic hormone from serum is likely to prove far more accurate than its extraction from urine. The above results, when amplified and confirmed, may therefore provide the necessary basic information for devising a reasonably accurate method for the bioassay of mammotrophic hormone in human serum.

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CONCLUSIONS

A mammotrophic hormone has been found in the serum of five healthy premenopausal women.

The experiments used for the identification of this hormone were designed also to provide information on the site of its production.

They suggest that it is produced by the anterior pituitary.

The Armour Laboratories, Kankakee, U.S.A., kindly supplied the sample of prolactin used in these experiments; 1 mg. contains 21·8 international units of prolactin by pigeon-crop assay. The preparation has not been assayed for growth hormone. We have evidence, however, that it contains a small but biologically active amount of this hormone.[3]

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New Inventions

MODIFIED TRACHEOTOMY TUBE

TRACHEOTOMY has been advocated for acute respiratory embarrassment in many conditions, both medical and surgical. Except for repeated bronchoscopy, it is the method of choice in keeping the large bronchi clear of secretions, for all that is required is the passage of a catheter through the tracheostoma. Unfortunately, the accumulation of secretions within the smaller branches of the bronchial tree cannot be reached by means of a catheter, and so may give rise to small areas of atelectasis, infection, and bronchopneumonia. So that the smaller divisions of the bronchial tree may be cleared effectively, the secretions must be coughed up into the larger bronchi. They may then be removed by means of a catheter. Patients with tracheostomies, however, cannot cough effectively because they cannot build up the requisite intrathoracic pressure, since the larynx is partly deprived of its natural function. In the conscious adult this disadvantage may be obviated by asking him to inspire, when coughing may then be made effective by occlusion of the tracheostomy. But smaller children, and especially infants, will seldom cooperate in this manner. Even if they do, the respiratory rate is much higher and it is difficult to correlate occlusion of the tracheostoma with the inspiratory and explosive efforts of the child. Occlusion of the tracheostoma at the wrong time will cause a feeling of suffocation, and the increased negative pressure in the alveoli may cause further alveolar collapse.

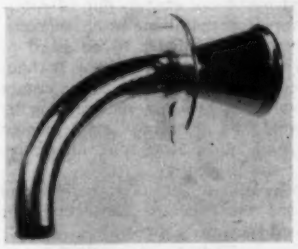

Fig. 1—Inner tube.

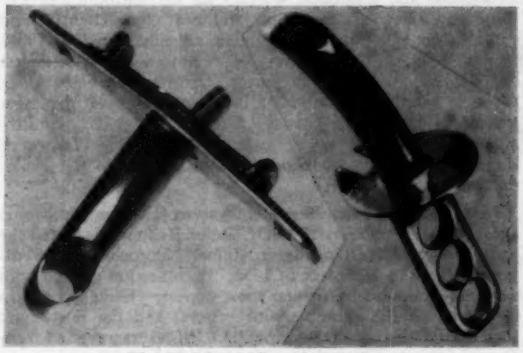

Fig. 2—Outer tube and occluder.

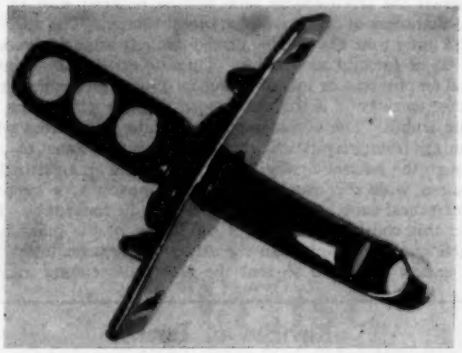

Fig. 3—Occluder in position in outer tube, showing restoration of anatomical airway.

With the above factors in mind, it was decided to modify the tracheotomy tubes in present use. The Alder Hey tube consists of an introducer, outer and inner tubes, and an occluder. The introducer requires no description, being similar to the standard pattern. The inner tube (fig. 1) also resembles the standard pattern, and consists of a hollow curved metal cylinder open at both ends. The superior end of this tube, however, is drawn out to a diameter much wider than the part which rests in the trachea. The outer tube (fig. 2) differs in that a hole has been bored on the superior aspect so that it lies in direct line with the aperture in the lower end of the tube. The occluder (fig. 2) is a solid metal cylinder, and fits in the outer tube when the inner tube has been removed.

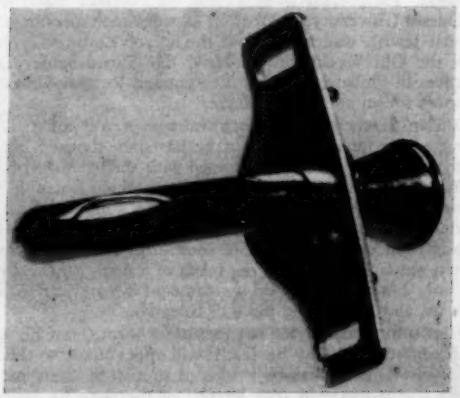

Fig. 4—Inner tube lying within outer tube.

The occluder, when inserted, restores the normal anatomical airway (fig. 3). If the child is trying to cough, either spontaneously or after stimulation by a catheter, the inner tube may be quickly removed and the occluder inserted. The normal airway being thus restored, coughing will be instantly effective, provided the laryngeal orifice is not completely occluded. Any sputum produced may then be expectorated through the normal channels or collected from the larger bronchi by means of a catheter, on removal of the occluder. The inner tube may then be replaced (fig. 4). This method therefore has the advantage of restoring the normal anatomical airway, which may again be converted into a tracheotomy in a few seconds. Any secretions collecting from the pharynx above the tube will also be expectorated, and the danger of their running down

alongside the tracheotomy tube will be reduced without the unpleasantness of repetitive pharyngeal suction. The aperture in the inner tube has been so placed that any attempt to cough will be as forceful as possible. There is no danger of interstitial emphysema or loss of power in coughing resulting from leakage as there is if the tracheotomy tube is bifid along the entire length. The occluder may of course be inserted when weaning from respiration through a tracheostoma to that through the natural airway. If for any reason an anæsthetic is required with the usual tracheotomy apparatus, a cutdown endotracheal tube has to be inserted into the inner tube. In a child this considerably reduces the lumen of the inner tube, which is already small. In the Alder Hey tracheotomy tube the end is expanded so that the anæsthetic tubing may be directly connected with no danger of reduction of the diameter of the airway.

This type of tracheotomy tube may be especially useful in tracheobronchitis, pneumonia, stove-in-chest injuries, and after chest operations.

The tube may be obtained for children or adults from Elliots Scientific Instruments, Ltd., Buckland Street, Liverpool, 17.

I wish to thank Mr. A. Rutana, registrar in ear, nose, and throat surgery at Alder Hey Children's Hospital, Liverpool, for allowing me to use this tube in his patients, and for his kind advice and criticism. My thanks are due to Mr. F. T. Howells of Elliots Limited, who made this tube to my specification, and to Mr. Rodney R. Green, photographer to Alder Hey Children's Hospital, who took the photographs.

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Reviews of Books

My Life with the Microbes

SELMAN A. WAKSMAN, PH.D., director, Institute of Microbiology, Rutgers University. London: Robert Hale. 1958. Pp. 320. 21*s.*

THIS is the autobiography of the scientist who has earned himself a place in history by his discovery, in September, 1943, of streptomycin—the first antibiotic shown to be of value in the treatment of tuberculosis. He is less widely known as the originator of that useful addition to our vocabulary, "antibiotic".

He was born in 1888, in a small township in the Russian Ukraine. He prepared himself for the entrance examination of Odessa University, but met on all sides such discrimination against Jewish students that, at the age of 22, he resolved to quit the Old World for the New. He joined some distant relatives in Philadelphia, and then entered Rutgers University to study for an agricultural degree.

Within a few years the new science of soil microbiology attracted his interest, and to it he has since devoted his life. His first monograph was concerned with the characteristics of a little-known group of microorganisms, which resemble both bacteria and fungi in some features, but which are, in fact, distinct from both—the actinomycetes. Eighteen years later it was from cultures of one of these organisms that streptomycin was isolated—not as the result of a single stroke of good fortune, but as the logical outcome of a carefully devised, tedious, and painstaking piece of research.

His enthusiasm for his subject shines throughout his book. One consequence may be that it will appeal more to the bacteriologist and laboratory worker than to the clinician; but every doctor can read with interest of the steps by which an impecunious immigrant in a strange land, with scarcely enough English to make himself understood, became one of America's most notable scientists.

Cerebral Palsy in Childhood

GRACE E. WOODS, M.D., deputy medical superintendent, Hortham Hospital. Bristol: John Wright. 1957. Pp. 154. 27*s.* 6*d.*

SEVERAL books on this subject have lately appeared; and this, the elaboration of an M.D. thesis, is an outstanding one. It is notable for the precision of its text, and clinical description and examination are particularly clearly set out. Unusual terminology is avoided; indeed, quite ordinary abbreviations are translated at the beginning.

The patients described came from a circumscribed area of England and they were mainly over the age of 5 years. The six principal clinical groups of cerebral palsy are effectively described; and ætiology as well as probable physical disability are summarised. Dr. Woods does not stop there, however, and she goes very fully into possible defects of special senses.

There is no attempt to discuss treatment or education, but the description of the assessment of educability is clear and will be a help to others interested in the vital matter of cerebral palsy, which affected 1·9 per 1000 live births attaining the age of 5 years in Bristol during the past decade.

Methods in Surgical Pathology

HENRY A. TELOH, M.D., assistant professor of pathology, North-Western University Medical School, Chicago, Ill. Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1957. Pp. 127. 36*s.*

INTENDED for the trainee in pathology, this book is a detailed guide to the naked-eye inspection of surgical specimens in the laboratory and the preparation of blocks for diagnostic histological examination. Emphasis is laid on providing the surgeon with useful and prompt information; and methods of dealing with various surgical specimens are given systematically in 28 chapters. Other chapters deal with more general topics, including operating-room techniques, tissue bacteriology, and prognosis. The author recommends the pathologist to prepare frozen sections personally, and gives two of his own techniques. Not all morbid histologists may agree with Dr. Teloh that careful naked-eye examination of specimens is often more satisfactory than examining frozen sections.

In this country trainees are now unlikely to be asked to prepare blocks for section from surgical specimens without first being instructed by demonstration, followed by constant supervision of this important task; but personal teaching by experienced pathologists would be effectively supplemented by this book. An appendix sets out in detail some illustrative reports, including histology and diagnosis.

The book should be read by all pathologists in training, and it will also interest surgeons who wish to learn about the methods of examining excised specimens.

Fossil Men (London: Thames & Hudson. 1957. Pp. 535. 84*s.*).—The fourth French edition of the world-renowned textbook of human palæontology by Prof. Marcellin Boule and Prof. Henri Vallois is here well translated by Michael Bullock in almost impeccable English, well subedited, and profusely and intelligently illustrated to tell the story of discoveries of fossil bones and implements of primitive man throughout the inhabited world. In his introduction Dr. Kenneth Oakley says that it is "the most comprehensive and authoritative general work on human palæontology" and tells us that Professor Boule "was originally one of the strongest opponents of the view that the Piltdown jawbone belonged to the same creature as the human braincase," and that Professor Vallois is "the leading exponent" of the view that "primitive *Homo sapiens* came into existence during Middle Pleistocene times, and evolved independently but parallel to the Neanderthal type".

Metabolism of the Nervous System (London: Pergamon Press. 1957. Pp. 581. £5).—Dr. Derek Richter has edited the proceedings of the 2nd International Neurochemical Symposium, held in Denmark in 1956. Each section opened with a review, followed by several short papers. The emphasis in 1956 was on the adult nervous system, and the relation of metabolism to structure and function. Speakers attended from Europe, North America, the Soviet Union, and Japan.

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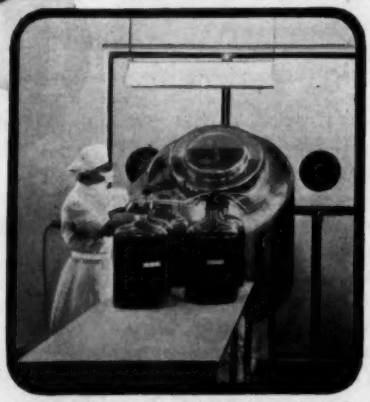

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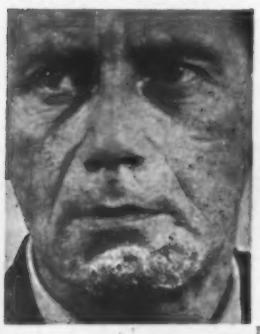

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THE LANCET

LONDON 15 MARCH 1958

Suicide and the Law

ONE of the more archaic laws in this country is that by which attempted suicide is a criminal offence. Scotland and most other countries seem content without such a law, and in France it was abolished as long ago as 1790.

The origins of this local taboo, now reviewed by Prof. GLANVILLE WILLIAMS,[1] are not entirely creditable: the inherent sinfulness of suicide seems to rest on shaky theological foundations, while its legal punishment originated largely in the convenience of making a suicide's property forfeit to the Crown. Not only have there been other countries in which suicide has been approved, but there are also circumstances in which our own culture approves it. That Captain OATES should give up his life in the way he did was generally recognised as an act of courage, setting a fine example. If the same criteria were applied to the depressive, his motives likewise might win respect; for he too believes that others will be better off without him.

Law and custom have undergone many civilising changes since the public dishonouring of the corpse in the 17th century; but vestiges of an older time remain, notably among some of the representatives of Religion and Law. Many attempts at suicide are not made known to the police, but in London at least the duty is still laid on ambulance men to notify all their cases, except those which have come to the notice of the patient's own doctor. Where a serious injury has occurred it is reasonable for the police to satisfy themselves on the facts, but to put a disturbed patient on a charge (before or after treatment), or to place a constable by his bed, is not helpful. Still less is it helpful to incarcerate the mentally ill in prison: this seems to us the very worst way of bringing about the social rehabilitation that such patients need. And there seems no doubt that would-be suicides committed to prison *are* mentally disturbed: Dr. EPPS showed this in her study of 100 consecutive admissions of attempted suicides to Holloway Prison,[2] and we believe that her experiences are the rule rather than the exception. Her important findings suggest, too, that the law does not work effectively as a deterrent; and we may note that Scotland (with no law against suicides) has only 45 suicides per million, compared with 79 in England.[3] Could it be that unconscious mechanisms, such as resistance or desire for punishment, make suicide more likely where it is forbidden?

One of the most alarming aspects of this law is the irregularity with which it is applied. Some police forces do not prosecute where there is any responsible relative or friend,[4] and local superintendents have remarkable powers of discretion in deciding whether or not to bring a charge. In 1955, out of 5220 attempted suicides known to the police, 43 were imprisoned: the figures for 1956 are much the same. WILLIAMS asks pertinently what principles are used in selection, or whether this depends entirely on the idiosyncrasy of judge or magistrate.[5] Perhaps the strongest argument for the existing law is that it obliges some recalcitrant cases to receive treatment; and Dr. R. I. MILNE,[6] a London coroner, has declared that medical treatment is aided, rather than hampered, by the activities of magistrates and police. Nevertheless it seems to us that, without the aid of criminal Law, most of the determined suicidal patients could be persuaded to enter hospital for treatment, and on the rare occasions where a patient cannot be so persuaded recourse can be had to mental certification. Some compulsory powers are still needed, but these are much better related to the therapeutic services than to the punitive. It is surely significant that in the recent correspondence in *The Times*[7] no voice was raised decisively in defence of the present law. In the House of Commons, Mr. BUTLER, the Home Secretary, said he had no evidence that an alteration in the law would be acceptable to public opinion.[8] *The Times*, however, believes that the public has no opinion,[9] and this seems to be largely true: there is no general feeling about suicide comparable to that on, say, the death penalty or the punishment of sexual offences. A motion tabled by Mr. KENNETH ROBINSON on Feb. 27—that suicide be removed from the category of criminal offences[10]—has scarcely added a ripple to the turbulent waters of Fleet Street.

It seems clear that this outdated law is as inconsistent and inequitable in its application as it is damaging in its effects. Its virtues are hard to discover: its vices are blatant. The sooner it is done away with the better.

Precision and Prediction in Hæmophilia

DEVELOPMENTS in technique are bringing quantitative precision to the exploration of blood-clotting defects in hæmophilia and related syndromes. These quantitative estimates enable better forecasts to be made about the likelihood of severe bleeding, whether spontaneous, or following mild trauma, or after, say, dental extraction or tonsillectomy. The methods used have also uncovered unexpected new facts, some of them difficult to explain. It has long been known that if, in a hæmophilic patient, the blood-clotting time was thirty minutes or longer, the patient was liable to spontaneous hæmorrhages, hæmarthroses, and severe bleeding after trauma; but if the clotting-time was less than thirty minutes, even if only a little longer than normal, it could not be assumed that the patient would be only mildly affected and that, for example, a tooth could be extracted with minimal precautions. A survey by BIGGS and MACFARLANE[11] of investigations of clotting function in 187 cases of hæmophilia and related syndromes contains much

1. Williams, G. The Sanctity of Life and the Criminal Law. London: Faber & Faber, 1958. Pp. 319. 30*s*.
2. Epps, P. *Lancet*, 1957, ii, 182.
3. Williams, G. *op. cit.* p. 247.
4. Williams, G. *op. cit.* p. 249.
5. Williams, G. *op. cit.* p. 251.
6. *Times*, Feb. 20, 1958.
7. *ibid.* Feb. 11, 20, 21, 24, 25, 26, 1958.
8. See *Lancet*, Feb. 15, 1958, p. 384.
9. Leading article, *Times*, Feb. 26, 1958.
10. See *Lancet*, March 8, 1958, p. 539.
11. Biggs, R., Macfarlane, R. G. *Brit. J. Hæmatol.* 1958, **4**, 1.

interesting information and reflects the present increasingly quantitative outlook.

Classical hæmophilia is now "disintegrated into a number of distinct entities with a similar symptomatology"; BIGGS and MACFARLANE's group included 138 cases of hæmophilia, 20 of Christmas disease, and 3 of ROSENTHAL's [12] syndrome of deficiency of "plasma thromboplastin antecedent" (P.T.A.); they also studied a few cases of other syndromes in which deficiency of antihæmophilic globulin had been found, including cases in 11 families with von Willebrand's disease. In 115 of their hæmophilic patients they assayed quantitatively the deficiency of antihæmophilic globulin in the plasma.

The techniques,[13 14] which are not simple, are based on the thromboplastin-generation test. This test uses: (1) a plasma fraction treated with specially prepared aluminium hydroxide which absorbs prothrombin, Christmas factor, and factor VII, and leaves antihæmophilic globulin and factor V; (2) serum which contains Christmas factor and factor VII; and (3) a suspension of platelets. When these three reagents are mixed and incubated at 37°C in the presence of ionised calcium, thromboplastin is formed; the amount of plasma-thromboplastin formed is estimated by adding some of the incubated mixture to a substrate of normal citrated plasma in the presence of calcium and observing the clotting-time—normally about ten seconds—of the substrate plasma. In hæmophilia the alumina-plasma will be lacking in antihæmophilic globulin, so thromboplastin generation will be defective and the clotting-time of the substrate plasma will be prolonged. By comparing the prolongation of the thromboplastin-generation test with a similar effect produced by diluting normal plasma, it is possible to estimate the diminution of antihæmophilic globulin in the hæmophilic patient's plasma as compared with normal plasma.

BIGGS and MACFARLANE thus found that, of their 115 hæmophilic patients, 63 had no detectable antihæmophilic globulin at all, and the remaining 52 had various levels up to 49% of normal. The group with no detectable antihæmophilic globulin included all except 1 of the severely affected patients in their series, and any patient with less than 10% needed blood-transfusion after tooth extraction or tonsillectomy. BIGGS and MACFARLANE point out that "it is fairly safe to say that a patient who has had teeth extracted on two occasions without bleeding for more than one week or who has had an uneventful tonsillectomy is unlikely to have the mildest degree of hæmophilia." But 6 of their patients with between 15 and 48% antihæmophilic globulin did not need transfusion after tonsillectomy, though 1 with 22% and 1 with 25% had to be transfused. They conclude that 5–10% antihæmophilic globulin protects against ordinary everyday stresses, but as much as 30–40% of normal is required to stop bleeding from major wounds or surgical operation sites; this involves giving a lot of blood.[15] It is this sort of evidence that leads BIGGS and MACFARLANE to conclude that the severity of the hæmophilic defect is closely correlated with the blood level of antihæmophilic globulin, and that consequently the estimation of this level is of great value in prognosis and the control of treatment.

12. Rosenthal, R. L., Dreskin, O. H., Rosenthal, N. *Blood*, 1955, **10**, 120.
13. Biggs, R., Macfarlane, R. G. Human Blood Coagulation and its Disorders; p. 423. Oxford, 1957.
14. Biggs, R. *Lancet*, 1957, ii, 311.
15. *ibid.* 1957, i, 376.

In the other syndromes studied, quantitative methods have so far proved less clearly helpful. In Christmas disease the factor is completely absent in all except the mildest cases, where the levels are 0–20% of normal. In von Willebrand's disease the observed deficiency of antihæmophilic globulin in 8 patients varied from 1·6 to 26% of normal, and they had prolonged bleeding-times as well. In ROSENTHAL's P.T.A. deficiency there is the curious combination of prolonged clotting-time, an abnormal prothrombin-consumption test, but nearly normal results with the thromboplastin-generation test; the cases are too few yet for precise estimation—BIGGS and MACFARLANE had 3 in their series—nor is the clotting defect clear, though SHARP [16] has suggested that it is lack of "viscous metamorphosis of platelets" in the earliest stage of the clotting process.

NOUR-ELDIN and WILKINSON [17] have set out evidence that another factor besides lack of antihæmophilic globulin or Christmas factor is linked with the severity of these diseases. This factor is an anticoagulant which they have detected in the plasma of patients with hæmophilia or Christmas disease, and its presence appears to be part of the inherited clotting abnormality. Using the current eponymous fashion, they call this factor "Bridge anticoagulant" after the first patient in whose plasma they detected it. Bridge anticoagulant was found, and its activity estimated, by using a variation of the thromboplastin-generation test described above. NOUR-ELDIN and WILKINSON found that if they used the patient's *own* citrated plasma as the test substrate, the clotting-time of the mixture was *longer* than when normal plasma was used. This effect might have been attributed to the deficiency of antihæmophilic globulin in the patient's plasma; but when they compared the results of using undiluted plasma or plasma diluted 1 in 5 as a test substrate, they found that the clotting-times were *longer* with the *undiluted* than the diluted plasma—the reverse of what would have been expected if deficiency of antihæmophilic globulin was responsible for the effect. The results could be explained by the presence of an anticoagulant, which would, of course, be less effective when diluted. NOUR-ELDIN and WILKINSON have found this Bridge anticoagulant in the plasma of each of the 109 patients with hæmophilia and 14 with Christmas disease so far tested; the anticoagulant did not remain active in the serum. The activity of Bridge anticoagulant can be estimated by the effect of prolonging the substrate clotting-times in the thromboplastin-generation test; the greater the difference between the clotting-times when normal and when patient's plasma is used as substrate, the greater the activity of the anticoagulant. They found that the more active the anticoagulant, the severer the clinical manifestations of the disease.

For example, a patient aged 32 had a whole-blood clotting-time of sixteen and a half minutes; he had had spontaneous bruising, melæna, epistaxes, and hæmarthroses; the thromboplastin-generation test substrate clotting-times using normal and his own undiluted plasmas were eighty-two and two hun-

16. Sharp, A. A. *Brit. J. Hæmatol.* 1958, **4**, 28.
17. Nour-Eldin, F., Wilkinson, J. F. *ibid.* p. 38.

dred and four seconds respectively. Another patient, aged 10, had a clotting-time of nine and a half minutes; the substrate times with normal and with patient's plasmas were twenty-seven and thirty-three seconds, and this patient had no spontaneous hæmorrhages though he bled excessively after trauma.

Anticoagulants have been reported in hæmophilia before, notably by TOCANTINS [18] and his co-workers; but the properties of the Tocantins anticoagulant are quite different from those of Bridge anticoagulant, nor does Bridge anticoagulant link up with the type of change described by HOUGIE.[19] The Bridge anticoagulant does not fragment the hæmophilia syndrome, but actually provides a link between classical hæmophilia and Christmas disease. It will be very interesting to see whether it is found in other members of the hæmophilia syndrome; NOUR-ELDIN and WILKINSON hint that it is absent in von Willebrand's disease. Fortunately the activity of Bridge anticoagulant can be estimated by a slight variation of the technique used for estimating antihæmophilic-globulin deficiency. Neither test can be satisfactorily undertaken by the routine laboratory that has few of these patients to deal with. It is now all the more important to send patients with suspected hæmophilia, especially children, to one of the special units, because, with these tests, they can give a reasonably accurate answer to the anxious parents' question: Will my child be severely or mildly affected? The answer may well affect the arrangements for schooling and future occupation.

Occupation and Health

THE publication of the Registrar General's Supplement on Occupational Mortality is always an important event; and, because war prevented the conduct of the decennial Census due in 1941, the report on the experience of mortality by occupation in the five years 1949–53 has special interest. The pivotal Census years of 1931 and 1951 represent the pit of economic depression and the full development of a Welfare State. Between lies a social revolution which might be expected to have altered the relationships of the risk of death in the different strata of society. In the latest report,[20] as in its forerunners, the population is divided according to occupation, and these occupations are grouped, according to the levels of education and social standing rather than income, into the five social classes: I, professional; II, managerial; III, skilled; IV, semi-skilled; and V, unskilled. In 1931 the mortality experience of men in these five social classes was compared with that of their wives, so that risks specific to the husband's occupation could be isolated from any general effect on health of the social and domestic environment or habits which they have in common. The same technique has been followed in the 1951 Census; and the changes in the work pattern of married women give fresh point to the comparison of present and past experience.

18. Tocantins, L. M. *Blood*, 1954, **9**, 281.
19. Hougie, C. C. *J. clin. Path.* 1953, **6**, 30.
20. Registrar General's Decennial Supplement, England and Wales, 1951, Occupational Mortality Part II. H.M. Stationery Office, 1958. 2 vols. £7 7s.

The introduction to the latest report reflects a certain sobriety about the interpretation of death-rates by occupation as obtained by current methods.

An excessive death-rate in a particular occupational group compared either with other men or with their own wives need not imply a specific occupational hazard. Men are drawn to certain jobs because they feel that they have the vigour to undertake them or because the jobs offer a sheltered environment for the less robust. After initial recruitment to the more arduous tasks in the community, the subsequent wastage of the weaker men leaves a more resilient group of survivors whose mortality experience reflects their superior physique rather than the stresses of their working environment. As a result, the prescribed practice of allocating a death to the last occupation of the deceased man, rather than to the occupation in which he has spent the bulk of his working life, leads to understatement of the hazard which the latter may present. On the other hand, particularly in industries such as mining where the specific mortal risks are well known, the informant at the time of death registration may not describe the deceased man as he was employed at the time of his death but according to his previous job—e.g., as a coalmine face worker. Again, both at census and at death, there is a tendency for men to describe themselves or others as employed on work with rather higher social prestige than the task actually performed: the fireman becomes a miner, the surface worker at the mine becomes a face worker, and so on. Because "promotion" effects of this type are present at both census and death the resultant errors in the death-rates by occupation may not be great; but the Registrar General refers to studies in the mining industry, carried out with his help and the cooperation of the National Coal Board at the London School of Hygiene and Tropical Medicine, which suggest that errors in job description and classification may be important in any detailed survey of death-rates in specific mining occupations.

The mortality experience of men's wives gives some indication of the effects of the immediate domestic environment. Broad regional differences in living conditions are illuminated by comparisons of social-class death-rates in different regions of the country. But the incidental risks of an occupation—e.g., the opportunities for excessive drinking among bartenders—are less easily identified. All these sources of consistent bias must, as the Registrar General emphasises, be remembered in interpreting the death-rates by occupation set out in this report.

Perhaps the most striking divergence between the 1931 and 1951 periods is in the overall trend in social-class mortality. In 1931 the death-rate rose consistently with descent of the social scale from class I to class V: in 1951 the W-shaped distribution of these rates results from the greater relative improvement in social classes II and IV—i.e., the managerial class and semi-skilled workers. Some of this disparity may be due to slight changes in classification, and some adjustments made in the report suggest that the low rate in social class IV can be thus explained. The reversal of the positions of social classes I and II cannot, however, be similarly accounted for; and the new superiority of the managerial class is shared by their wives.

Of the individual causes of death which make up these social-class differences in total death-rates, some follow the 1931 trends by increasing steadily in frequency in both sexes from social class I to V—tuberculosis, syphilis, cancer of the stomach, bronchitis, and pneumonia. Cancer of the lung has a similar trend only for males; the trend is reversed in females. Of the other neoplastic diseases, cancer of the uterus and breast have the contrary trends with social class which

are already familiar, while leukæmia mortality falls consistently from social class I to V. A summary of the gains and losses in social classes I and II suggests that their relative position has been altered by an increased mortality in social class I from coronary-artery disease, tuberculosis, accidents, cancer, vascular lesions of the central nervous system, and chronic endocarditis and a relative decrease, largely in cancer and bronchitis, in social class II.

The detailed account of the social and occupational patterns of the various causes of death will doubtless form the pabulum of many future essays on social medicine. From the *embarras de richesse* purveyed in two large (and rather expensive) volumes, some biased sampling produces data of interest in more than one disease. The changing epidemiological behaviour of coronary-artery disease, for example, has excited much controversy on the role in its ætiology of diet, exercise, smoking, and stress. The continuing increase in the reported death-rate is unlikely to be entirely due to increasing diagnostic skill or changes in classification; and there is some consistency between the 1931 and 1951 Census in the male social-class gradient from its peak in the professional group. The low death-rates from coronary-artery disease among the manual workers in the population would fit in with the idea that physical exercise is a powerful prophylactic against this disease. In married women aged 20–64, on the other hand, the highest rates are among the wives of the manual workers. Indeed the pre-war social gradient of mortality in both sexes which was compatible with the dietary-excess theory of causation has now been upset by this reversal in women. Psychological explanations of coronary-artery disease may be somewhat under a cloud; but there is perhaps food for thought in the observation that, while the excessive death-rate early in life among senior Civil Servants may be part of the price of a Welfare State, occupational opportunities for exercise have not prevented the small group of professional cricketers, footballers, golfers, &c., from having a standardised mortality ratio 73% above the national average.

An interest in the experience of our own profession need not be dismissed as mere hypochrondriasis. Among the 34,000 medical practitioners alive about the time of the Census there were reported 1008 deaths instead of the 1129 expected at the rates for all males. This gives a standardised mortality ratio of 89, which is less than the ratio of 106 reported for 1930–36. The introduction of the National Health Service thus does not seem to have been associated in time with an excessive mortality from all causes. Doctors certainly have a standardised mortality ratio from coronary-artery disease of 159, but this differs little from the ratio of 152 for ministers of religion and not greatly from the value of 120 for dentists and 121 for members of the legal profession. In the same way, although medical practitioners have an excessive number of deaths from poliomyelitis, this excess is equally evident among judges, barristers, and solicitors. Of the remaining causes of death, only leukæmia, vascular lesions of the central nervous system, and suicide are much above the national average.

In this report there are countless intriguing indications for further research in both occupational and general medicine. Even if only a few such clues are successfully followed up, the General Register Office will not have laboured in vain.

Lord of Misrule

ACADEMIC apathy is a complaint that is often flung at the students of today; but the words cannot justly be applied to the lively proceedings at Glasgow last month. In the Scottish universities the election of a lord rector, the official representative of the student body, is often a vigorous affair, and his installation is an occasion when both licence and toleration are traditionally exercised. But it is unusual for a Minister of the Crown and university and civic dignitaries to have to withdraw from the platform, bearing on their persons and gowns the unmistakable traces of unorthodox if misdirected missiles. The press who had come to record the words of the Secretary of State for Home Affairs remained to report the students' exertions, which next morning were the subject of conversation in tube, bus, and train and of a leader in *The Times*. Nobody could say that the students had, or deserved, a good press; but the feeling gradually gained ground that the incident was better left to academic and local reprimand than dealt with by national ukase.

Nevertheless, the general question of student turbulence, why it persists, and whether it should, is of interest to us all. At Glasgow the outbreak was aggravated by extraneous circumstances—the similar occasion at Edinburgh the day before, the Rochdale by-election, and the political personality of the new rector—but the episode is not an isolated one. The Scottish universities, perhaps because of their long association with the universities of the Continent, have retained most firmly the medieval tradition of festivals of acknowledged horseplay at which the sway of the Lord of Misrule is, by some reluctantly, accepted. But even south of the Border students have not entirely discarded these practices, and some, within the last few weeks, have rudely interrupted the performance of a pantomime. These incidents are more likely to disturb, inconvenience, and annoy other people, and thus achieve publicity, in large cities where the university is a small part of the community. But in the comparative privacy of the more secluded universities students have been known, though admittedly with less disturbance to the town, to use the calm of their cloisters for rites which form no part of the courses of study arranged for them.

To understand, though not necessarily to support, these bouts of unreason and physical activity, we must consider the peculiar difficulties of the student. His life, like so many other lives, is not easy. Most of these young people are working hard; for today the student who does not pass his examinations does not remain at the university, and in every faculty the curriculum grows no lighter. Most of them are fairly hard up and

many of them add jobs in the vacation to term-time studies. More important perhaps, their entrance into workaday life has been delayed. They see many of their contemporaries started on their careers, earning money, and assuming adult responsibilities, while they still live in a state of semi-tutelage and semi-responsibility, still dependent on others—whether parents or State—for their board, keep, and pocket-money. To stand on the brink of a swimming-pool, or of life, is a jittery business, especially if you are not yet sure how well you can swim; and something of the tension of these uncertain strenuous years has been shown in the reports of the student health services.[1] Its occasional release, even though sometimes over-violent, is usually well tolerated, and the pleasantest part of the Glasgow ceremony was Mr. BUTLER's ready assumption of his new duties as lord rector and his championship of his new constituents.

But these young people are the selected brains, and brawn, of the country. They have surmounted every educational hurdle from the 11+ onwards, and it is surely not beyond their wit to modify old customs and to find opportunities for robust relaxation which will not injure other people or their property. Their fellow citizens, for instance, would have nothing but amused admiration for any good-tempered masquerade or well-planned exploit such as the visit of a party of unusual European royalty to a London hospital sports ground.[2] If the Lord of Misrule is to retain his place on the staff of the university health services, it is time for him to exchange his cap and bells for his thinking-cap and to devise new forms of therapy for his subjects.

Annotations

NEW SOURCES OF FOOD

HALF the world is underfed, and the population still increases faster than its food-supply. Temporary surpluses in a few favoured countries should not mask the real world shortage; for the disparity between the better-fed and the worse-fed nations is actually widening. Mr. N. W. Pirie, F.R.S., made these points in the lecture he was giving to the Royal Society of Arts last Wednesday,[3] and outlined means of producing more food—especially protein. In the past, production was increased largely by cultivating virgin lands; but none of those remaining are comparable to the areas opened up in the 19th century. We could raise the output per acre (1) by improving the breed of plants, (2) by supplying more light, heat, and water (here cheap nuclear power may help, though it creates its own problems), and (3), more profitably, by using more fertilisers, especially in South and East Asia. But Mr. Pirie devoted most of his attention to prevention of waste.

This involves not only the control of diseases and pests, and making use of material now rejected, but also the avoidance of losses on conversion. At present we use animals for conversion (i.e., of fodder to human food) and as a source of protein, though the animal adds nothing new and yields foodstuffs equivalent to only part of the vegetation it eats. The merits of the animal are: (1) that it provides a bigger ratio of protein to carbohydrate than does its fodder; (2) that the aminoacid composition of its protein is closer than that of some plants to what we believe suitable for man; (3) that it sometimes thrives on foods too fibrous for man; and (4) that animal foods are familiar and appeal to the palate. At Rothamsted Experimental Station, where Mr. Pirie is head of the biochemistry department, mechanical and chemical processes are being investigated which will separate from green leaves a substantial proportion of protein and other food elements direct, without using an animal as an intermediary. At present the separation is incomplete, and some protein remains in a fibrous residue which is used as fodder for animals; but in the future this residue might be less wastefully subjected to conversion by microorganisms than by animals. Useful enzymes (e.g., that convert cellulose to glucose) abound in Nature and might be pressed into man's service. Moreover, of hundreds of thousands of plant species known, only about a hundred at present contribute significantly to human nutrition. "Our choice is still restricted unreasonably by the whims and limitations of primitive man". We should be searching the plant kingdom for species which will grow exuberantly and which contain nutritionally useful components which new techniques would enable us to extract. Research on these lines is especially appropriate for Britain, where we have little land but much scientific and technical skill.

POSTOPERATIVE HYPOTENSION

HYPOTENSION in the postoperative period has been investigated by Barbour and Little [1] in close on 5500 patients. Taking a systolic pressure of 90 mm. Hg or less in a normotensive patient, and a fall of 40–60 mm. Hg in a hypertensive patient, as the criteria of an abnormally low pressure, they found that 1 in every 31 patients had a hypotensive episode.

No-one should doubt the potential dangers of a drop in blood-pressure at this time. Damage to the brain, perhaps discovered only at a later date from minor alterations in mental performance, death from sudden cardiac decompensation, and renal damage are recognised sequels, while vascular thrombosis and pulmonary embolism may in some measure be attributable to it. Elderly and ill patients are most likely to suffer ill effects if the blood-pressure falls, but those who are otherwise fit may suffer when unrecognised slight hypotension is accentuated by the sitting position or an unnecessarily large dose of a sedative drug.

The relationship between complications, early or late, and hypotension is unknown; routine recording of the blood-pressure immediately after operation is not common practice. Considering the immense amount of skill, care, and time nowadays given to each patient by a team of highly specialised people in the operating-theatre, it seems illogical that soon afterwards, at a time often of rapid physiological transition, the patient should be transported to another part of the hospital, and there, though observed for gross complications, rarely tested for the earliest premonitory signs.

Barbour and Little divide the causes in their series into six main groups—cardiovascular, respiratory, pharmacological, neurogenic, hæmatological, and humoral. The common causes include myocardial insufficiency from

1. Parnell, R. W. *Lancet*, 1951, i, 731; Malleson, N. *ibid.* 1954, i, 824.
2. Peripatetic correspondent, *ibid.* 1956, i, 346.
3. To be published in the journal of the society (6 John Adam Street, Adelphi, London, W.C.2).

1. Barbour, C. M., Little, D. M., Jr. *J. Amer. med. Ass.* 1957, **165**, 1529.

heart-disease; circulatory depression due to high blood-carbon-dioxide tension, associated with inadequate ventilation during anæsthesia; the effects of drugs, some of which exert their effect for many hours; and inadequately relieved pain. Occasionally the cause is less obvious, as when oligæmia from unobserved blood-loss during operation leads to postoperative hypotension (about 1500 ml. of blood can be lost during general anæsthesia without obvious change in the blood-pressure or pulse-rate [2]) or when a simple faint is precipitated by postural changes in a patient who has recently come round from an anæsthetic.[3] Quite severe hypotension may follow an operation and anæsthetic when the patient does not respond by the normal output of adrenocortical hormones, owing perhaps to previous treatment with cortisone or related steroids,[4] or perhaps to adrenal exhaustion after long or severe illness.

This investigation by Barbour and Little shows both that significant postoperative hypotension is relatively common, and that the patient should be kept near those who, from their knowledge of his behaviour during the operation and anæsthesia, can easily recognise changes in the recovery period. All of their patients were observed in a recovery-room, and most of those who were hypotensive needed blood-transfusion.

RE-STENOSIS AFTER VALVOTOMY

FIFTY-SIX years ago Lauder Brunton [5] first suggested the surgical treatment of mitral stenosis by "elongating the natural opening"; and at the time we expressed misgiving that [6] "the incision in such a valve would show a great tendency to unite directly and the state of the valve would then be worse than before". This doubt has hardly been confirmed in the ten years since mitral valvotomy was established. It might seem that fracturing or splitting the deformed valve must inevitably leave ragged, raw edges, inviting readherence of the cusps with subsequent stenosis matching the original in severity. Magarey [7] predicted that stenosis would recur after valvotomy because of thrombus formation on the irregular cusps, but Glover [8] has denied that it does. It is now evident that re-stenosis can take place in certain circumstances, but it is surprisingly uncommon; Belcher [9] has investigated its mechanism in eleven published cases and twelve of his own.

In all these cases improvement after the original valvotomy was not maintained, and at a second operation or necropsy refusion of the cusps was found. Belcher's findings suggest that the mobilisation of the valve cusps at operation is the crucial factor, and he emphasises that re-stenosis has not yet been seen where both commissures have been completely divided. In the majority of his own patients who needed a second operation, the valve had not originally been split beyond the critical areas of tendon insertion. These findings endorse the views of Brock,[10] who first emphasised the significance of the insertion of the main chordæ tendineæ. At these two sites, on either side of the central pathway of the mitral valve, the cusps are held most tightly in apposition during systole, and in Brock's view rheumatic adhesion first appears there; he termed them the critical areas of tendon insertion. The ideal valvotomy consists in division through these critical areas on each side, followed by splitting of the commissures to their lateral edges. In addition, the chordæ must be carefully separated from one another, and from the valve cusps, to ensure a maximum mobility. The pliancy of a valve [11] can often be deduced from auscultation, but until the heart is opened it is impossible to be certain how much can be achieved: fibrosis and calcification of the cusps, or fusion of the chordæ, may prevent more than slight separation, rendering the condition virtually inoperable; re-stenosis is likely to follow, even though some initial benefit is experienced. But if a calcified valve is suspected before operation, it does not follow that valvotomy is impossible. It is worth emphasising that a technically successful operation leads to disappearance or shortening of the murmur and a softer first sound.[12]

Smouldering rheumatic activity is invariably difficult to confirm, and how often re-stenosis is due to this is uncertain: Belcher thinks that when re-stenosis follows complete separation of the commissures it may be the result of rheumatic activity, and in 7 published cases of this type rheumatism could be blamed in 5. After a technically imperfect valvotomy readherence may quickly result from fibrin deposition alone.[7] It is clear that successful valvotomy depends at least partly on proper appreciation of the anatomy and pathology of mitral stenosis, and Glover et al.[13] have said: "it must be the pathological changes in the valve and not the surgeon's ignorance of an ideal valvotomy which limits the operative procedure"

HEREDITY IN ENURESIS

IT is not always clear at just what point an extensive family study of a particular clinical condition becomes worth while. Patients with enuresis may well be heterogeneous; suggested causes of the condition range from anatomical defects of the upper urethra to psychological immaturity. A family study might be expected to indicate whether there is an appreciable genetic element in causation; perhaps to isolate a small proportion of cases with strong genetic determination; and, more generally, to reveal subvarieties of the condition by the fact that these breed true within families—though the alternative, non-genetic, explanation—that any familial concentration is due to a family tradition—must always be borne in mind.

The tendency for bed-wetting to occur in families has been known at least since the end of the last century. Obviously the proportion of a series of patients who are found to have a relation of some degree or other affected will depend on how thoroughly the family is investigated; and estimates of the proportion of patients with a positive family history vary from 3% to more than 90%. Blomfield and Douglas [14] in 1956, with a near-perfect sample of English children, found that significantly more brothers and sisters of regular bed-wetters were also affected than were the brothers and sisters of children who were dry at night—10·6% compared with 5·1%. The family inquiry was made by health visitors with no special training in taking family histories, but the series is a very large one and the relative findings are acceptable. Dr. Bertil Hallgren,[15] of Stockholm, has re-examined this

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3. Bourne, J. G. *Lancet*, 1957, ii, 499.
4. Salassa, R. M., Bennett, W. A., Keating, F. R., Jr., Sprague, R. G. *J. Amer. med. Ass.* 1953, **152**, 1509.
5. Brunton, L. *Lancet*, 1902, i, 352.
6. *ibid.* p. 461.
7. Magarey, F. R. *Brit. med. J.* 1951, i, 856.
8. Glover, R. P. *Trans. Amer. Coll. Cardiol.* 1955, **5**, 209.
9. Belcher, J. R. *Brit. Heart J.* 1958, **20**, 76.
10. Brock, R. C. *ibid.* 1952, **14**, 489.
11. Sellors, T. H., Bedford, D. E., Somerville, W. *Brit. med. J.* 1953, ii, 1059.
12. Wood, P. Diseases of the Heart and Circulation. London.
13. Glover, R. P., Davila, J. C., O'Neill, T. J. E., Janton, O. H. *Circulation*, 1955, **11**, 14.
14. Blomfield, J. M., Douglas, J. W. B. *Lancet*, 1956, ii, 850.
15. Hallgren, B. *Acta psychiat., Kbh.* 1957, **32**, suppl. 114.

question in an admirably thorough survey in which he personally examined children and questioned their parents. Index cases were collected from the psychiatric department of two children's hospitals in Stockholm—111 patients from one hospital and 119 from the other. The series was probably somewhat selected for high frequency and late age at cessation of bed-wetting, and for persistent emotional disturbances; on the other hand, mentally backward children were probably under-represented. In about 15% of patients the enuresis was "acquired", in the sense that control had been gained and then lost again. There is good reason to suppose that anatomical defects play little part in the causation of the abnormality in such children. Of the 119 children from one hospital 105 were examined by urethrocystography, and 20 in whom further investigation seemed desirable underwent cystoscopy. Of these, 3 had minor anatomical abnormalities, which were treated without affecting the enuresis.

Hallgren finds that the family analysis does not distinguish between the two main clinical groupings—"nocturnal" enuresis and "nocturnal plus diurnal" enuresis. Any genetic predisposition is therefore common to both conditions. The data suggest that the family risks are higher for primary than for acquired enuresis; the difference is significant for the parents but not for the relatively few brothers and sisters. Grouping primary and acquired cases together the risks to parents and brothers and sisters is clearly higher than for the general population. Hallgren estimates the risks in the general population of Stockholm as 10% for nocturnal enuresis and 2% for nocturnal plus diurnal enuresis in boys; while for girls it is 6% and 2% respectively. He found that of 208 fathers 64 (33%) had been affected; and, assuming ascertainment by individual, of 129 brothers 40 (31%) had been or were affected; he also found that of 215 mothers 38 (18%) and of 133 sisters 25 (19%) had been affected. These proportions are between two and three times that in the general population. In the nine families where both parents had been affected, 7 of 10 siblings were also affected.

Genetic predisposition is perhaps likely to account for a greater proportion of this family resemblance than family tradition. A large twin study would help to establish the distinction. The nature of the genetic predisposition remains unclear. The reality of the other element—family tradition—is shown in Blomfield and Douglas' finding that bed-wetting is more prevalent in the lower social classes, and in urban than in rural children.

PROSPECTS IN THE PREVENTION OF BLINDNESS

THE comprehensive welfare services for the blind in this country have yielded much statistical information. Sorsby's reports [1–3] have been supplemented by his summaries in the annual reports of the chief medical officer of the Ministry of Health.[4] An outstanding problem revealed by these studies was the high proportion of cataract patients—about 25%—amongst those registered as blind. Some 80% of those registered as blind from cataract had not sought or obtained treatment. In 1954 the Ministry of Health made available more beds for cataract patients and sought to distribute the waiting-lists more evenly [5]; and now it has issued a direct appeal to general practitioners, who in the first place have charge of the potential cataract patient. A widely distributed memorandum [6] points out that the old teaching that operation could not be undertaken until the cataract was ripe is no longer valid, for by modern methods the cataract can be removed as soon as vision is seriously reduced. One difficulty is that no less than a third of new registrations of blindness relate to people over the age of 80; and, though cataract surgery at such an advanced age generally presents no special problems, in many patients operation might have been undertaken under better conditions at an earlier age. It is disturbing that, in spite of the general medical services available to all under the National Health Service and the recent expansion of ophthalmic departments, most of those seeking admission to the Blind Register apply through the National Assistance Board, and not through medical agencies.

Cataract is generally regarded as a "senile" affection, and so are the macular lesions misnamed senile macular degeneration. Together these two affections account for nearly 50% of all registrations of blindness. But out of altogether nearly 5 million aged over 65 years only some several thousands a year are affected by these lesions; the Ministry's memorandum rightly emphasises that old age by itself does not cause blindness, and the nature of these two affections is unknown. Little is known, either, of glaucoma, another major cause of blindness, which tends to affect younger patients. Though much can be hoped for from administrative action on cataract, there is little immediate prospect of reducing the incidence of blindness from senile macular degeneration or from glaucoma, but early diagnosis and treatment are essential in the management of glaucoma.[7]

Overall surveys—because of the high proportion of aged among the newly registered—necessarily emphasise cataract, senile macular degeneration, and glaucoma. A different picture emerges if attention is confined to the blind under the age of 50. Here optic atrophy stands out as the largest single group, with 22·6% of the total in 1955 and 23·0% in 1956; and among the specified causes of optic atrophy "pre-natal influences", intracranial lesions, and disseminated sclerosis were outstanding with a total of 65·8%, while in some 18% no cause was established. Optic atrophy therefore calls for urgent investigation if the amount of blindness in the age-groups under 50 is to be substantially diminished. Retinitis pigmentosa and its allied conditions, myopia, congenital defects, diabetic retinopathy, and iritis and iridocyclitis all account for a substantial quota of cases.

Any survey of the causes of blindness today shows that there are one major surgical problem—cataract—and a mass of medical problems. Traditionally ophthalmology is largely a surgical specialty; and the recognition that a substantial series of medical problems lie before it is in itself a considerable advance. Today the general practitioner is being urged to select his cases for surgical treatment, but he may be called on to play a more active part in the ophthalmology of the future.

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Special Articles

DISRUPTION OF MARRIAGE *
SOME POSSIBILITIES OF PREVENTION

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AT the Maudsley Hospital the front page of every patient's notes records whether he or she is single, married, widowed, divorced, separated, or extramaritally cohabiting. From this information I have compared the incidence of broken marriages in the three major diagnostic assortments comprised in Section V of the International List of Diseases and Causes of Deaths—namely, psychoses, psychoneurotic disorders, and disorders of character, behaviour, and intelligence. The findings, which at first may seem surprising, are shown in the tables. Table I sets out the three assortments, adding a fourth or miscellaneous assortment to accommodate patients whose diagnosis placed them outside the others. Table II shows a breakdown of the same number of patients into seventeen diagnostic groups that are included in the three major assortments.

TABLE I—NO. OF BROKEN MARRIAGES (DIVORCES, SEPARATIONS, AND EXTRAMARITAL COHABITATIONS) AMONG 7996 EVER-MARRIED INPATIENT AND OUTPATIENT DISCHARGES IN FOUR MAJOR ASSORTMENTS

(Years 1952–54, Bethlem-Maudsley Hospital, London)

Diagnostic assortment	Males			Females			Total		
	E.M.	D.S.C.	%	E.M.	D.S.C.	%	E.M.	D.S.C.	%
Psychoses	983	74	7·5	1638	122	7·4	2621	196	7·5
Psychoneuroses	1473	146	9·9	2290	235	10·3	3763	381	10·1
Disorders of character, &c.	542	109	20·1	228	64	28·1	770	173	22·5
Miscellaneous	390	38	9·7	452	36	8·0	842	74	8·8
Total	3388	367	10·8	4608	457	9·9	7996	824	10·3

E.M., ever married; D.S.C., divorced, separated, or cohabiting.

Among some 8000 patients who have been married (single patients are excluded from the figures) there were 824 broken marriages—an average of a little over 10%. But the distributions among the first three assortments vary notably. The lowest incidence of broken marriages (7·5%) is in the psychoses. In our series of over 2600 ever-married psychotics, patients with schizophrenia and manic-depressive illnesses constitute over two-thirds. The next highest incidence of broken marriages (10·1%) is found in the psychoneurotic disorders. To our series of over 3700 ever-married psychoneurotic patients, those with anxiety (in its many forms) and reactive depression contributed over two-thirds. But much the highest incidence of broken marriages (22·5%) is found in the assortment comprising disorders of character, personality, and intelligence. Among these, in our series, people in whom psychopathic and immature personalities had been diagnosed comprised 57%; but a substantial additional contingent was contributed by men with sexual deviations, and addiction to alcohol or drugs.

In this third assortment, women did relatively worse than men (table I). The marriages of over 28% of the women broke up, compared with a rate of just over 20% among men; and within this assortment the marriages of men with sexual deviations fared better than might have been expected (table II). There were 89 such men, among whom the marriages of a little over 12% had broken. This figure compares favourably with that of over 20% for all the men in the assortment. Among patients with sexual deviations, exhibitionists and homosexuals figure prominently. It can be surprising how often such men, apart from their abnormalities, make good husbands and have loyal wives.

Homosexual activities among women are not in British law a criminal offence. For this and other reasons fewer homosexual women than men seek treatment from doctors and hospitals. The same can be said about exhibitionism. Though the cosmetic industry, the strip-tease act, and everyday experience testify to the presence among women of impulses which could broadly be called exhibitionistic, these activities scarcely ever bring women into conflict with the Law. In thirty years' experience, I have dealt with only 1 female exhibitionist who sought medical treatment.

Before leaving this topic, I want to make two points clear.

First, these figures are not to be taken as in any way representative of the collective experience of Britain's mental hospitals. My hospital takes into its wards patients who are deemed to be remediable, though many are acutely ill. The 7996 ever-married psychiatric patients on whom the two tables are based were mostly referred to the hospital by doctors practising in the southern half of London; these patients are, as far as we know, a fair sample of the inhabitants of South London who become ill enough to be referred by their doctors to a psychiatric hospital for either diagnosis or treatment.

TABLE II—NO. OF BROKEN MARRIAGES (DIVORCES, SEPARATIONS, AND EXTRAMARITAL COHABITATIONS) AMONG 7996 EVER-MARRIED INPATIENT AND OUTPATIENT DISCHARGES IN SEVENTEEN DIAGNOSTIC GROUPS

(Years 1952–54, Bethlem-Maudsley Hospital, London)

Diagnostic group	Males			Females		
	No. ever married	Divorced, separated, and extra-maritally cohabiting		No. ever married	Divorced, separated, and extra-maritally cohabiting	
		No.	% of ever married		No.	% of ever married
Schizophrenic disorders	182	21	12	334	42	13
Manic-depressive reactions	466	30	6	781	49	6
Paranoia and paranoid states	52	5	10	55	12	22
Senile psychoses, &c.	90	1	1	120	4	3
Organic disorders of the nervous system	(42	3	7)	73	6	8
Other psychoses	151	14	9	275	9	3
Anxiety	483	41	8	605	42	7
Hysteria	108	16	15	247	36	15
Obsessive - compulsive reaction	86	4	5	103	10	10
Neurotic-depressive reaction	488	66	14	994	124	13
Other psychoneuroses	308	19	6	341	23	7
Pathological and immature personalities	278	60	22	164	47	29
Sexual deviations	89	11	12	(1	1	100)
Non-sexual delinquency or crime	(38	6	16)	(17	3	18)
Addiction to alcohol and drugs	137	32	23	(46	13	28)
Miscellaneous	379	36	10	439	34	8
Other groups with small nos. of patients	(11	2	18)	(13	2	15)
Total	3388	367	11	4608	457	10

Figures relating to totals of less than 50 are in parentheses. Percentages to nearest whole numbers.

* From a paper given at the first conference of the International Planned Parenthood Federation of the region for Europe, Near East, and Africa, held in West Berlin, October, 1957.

My second point is that the figures must not be taken as representative of broken marriages in general. Many marriages founder and break without the patients consulting either marriage-guidance services or doctors, and without their being referred to hospitals. When, for example, a married person falls in love with someone else and the marriage is dissolved, doctors and hospitals are unlikely to be involved. My figures are representative of a small segment only of the totality of broken marriages. They may, nevertheless, provide a basis for cautious generalisation.

The main point which emerges is that, among ever-married patients referred to hospital for a wide variety of psychological infirmities, marriages have proved most unstable among the assortment which comprises psychopathic and immature personalities. Why should this be? A possible answer is that an early or recurrent psychosis is commonly felt by the patient's spouse to be outside his control. It is treated as an affliction descending from without. The same may, to a lesser extent, be said of psychoneuroses, of which, as above remarked, over two-thirds were cases of anxiety or depression. Again the illness is commonly felt to be external to the patient, who commonly fights against it. But when a psychopathic or immature personality is diagnosed the position is different. The infirmity here is felt to be not a visitation from without but a factor of his essential personality. It is less a matter of *what the patient suffers from* than of what he *is*.

Psychopathy is less easy to define than either psychosis or neurosis. All I need say is that two types of psychopath are commonly recognised—the inadequate and the aggressive. Psychopaths are well described, in the report of the Royal Commission on the Law Relating to Mental Illness and Mental Deficiency, as people

> " whose daily behaviour shows a want of social responsibility and of consideration for others, of prudence and foresight and of ability to act in their own best interests. Their persistent anti-social mode of conduct may include inefficiency and lack of interest in any form of occupation; pathological lying, swindling and slandering; alcoholism and drug addiction; sexual offences, and violent actions with little motivation and an entire absence of self-restraint, which may go so far as homicide."

A diagnosis of psychopathic personality is made more often in men than in women.

The immature personality may have features in common with the aggressive, but typically retains the dependency, the egocentricity, or the silliness of childhood. I am myself in the habit of making either a primary or a supplementary diagnosis of immature personality as often in women as in men.

These general considerations of hospital experience may make it understandable why the marriages of people with psychopathic and immature personalities readily founder. I now turn to my own personal experience of those whose marriages, at the time I first saw them, had not actually broken. The marriages were under strain, and it was sometimes in the hope of preventing a rupture that the patient was referred to hospital.

I have asked myself what features of personality most often impair the happiness and stability of marriages. My answer (which as yet I should find difficult to support with figures) is first immaturity, then meanness (for example, over money), and then jealousy.

Immaturity takes two main forms. The first is characterised by excessive dependency, social timidity, and a sense of personal inferiority or inadequacy. These are accompanied by lack of confidence and an insatiable need for reassurance. The possession in common of these misgivings establishes a bond of sympathy between young people which can lead to marriage; but before long frictions develop, because each is making vain demands for reassurance and moral support from the other. A sense of disillusionment generates irritability and irrational feelings of grievance. Things are often brought to a head when either one partner or the other is attracted by someone of more assertive and self-reliant character.

The second kind of immaturity, perhaps commoner among women than men, has as its central feature an egocentricity which blinds the subject to the claims of others. Minor frustration or disappointment is followed by explosions and tantrums, often called hysterical, which are adult equivalents of the temper tantrums of childhood. Marriages thus strained may endure if the spouse is indulgent or pliable; but commonly the worm turns, and either the woman deserts the man, whom she regards as contemptible, or he deserts her regarding her as insufferable. Sometimes the marriage is sustained in a spirit of cold warfare.

I have found that *meanness* in a man will antagonise and estrange a woman more than will acts of violence. I have been astonished at the physical ill-treatment which some women will put up with from periodically intemperate husbands, provided that they later feel and express regret. The woman treats the outburst as somehow out of character and forgives it. Very different is her reaction to intractable meanness or jealousy. These are felt to be despicable traits, forming an integral part of the man's nature, which he makes no effort to combat. Affection and respect—the emotional mainstays of most marriages of people over 50—are slowly undermined and are replaced by hatred and contempt. Among patients more often than among those whose marital troubles do not bring them to doctors, marital jealousy is coloured by a paranoid suspicion. The jealous partner will ransack the pockets and diaries and steam open the letters of the suspected person in search of incriminating evidence. If the marriages of such persons do not break down, they are precariously sustained in an atmosphere of hostility which is one of the nearest approximations to hell-on-earth attainable in modern life.

These and certain non-clinical considerations have led me to the tentative view, which again I could scarcely substantiate with figures, that between 65% and 75% of men and women could, from the standpoint of a matrimonial agency, make good " general-purpose " husbands or wives. By this I mean that they would make good husbands or wives no matter whom they married, provided that the spouse also fell within the wide range of a good general-purpose husband or wife; that another 35–25% require a rather special kind of spouse to make a success of marriage; and that from about 1–3% are next to impossible as marriage partners no matter whom they marry. In suggesting these ratios, I have in mind that between 1% and 2% of people in most countries are sufficiently oligophrenic to be seriously handicapped, and that a large proportion of the deteriorated schizophrenics who spend their lives in mental hospitals are unmarried. I also have in mind the " psychopathic fringe ".

Possible Preventive Measures

How far are the factors conducive to the disorganisation of family life preventable? Perhaps they could be reduced to vanishing point by an enhanced knowledge and practice of eugenics and by improved educational programmes. These advances, however, are not yet in sight, and we should not be unreasonably hopeful. Nevertheless something can be done today.

Along eugenic lines much good could be done by the discovery and use of a perfect contraceptive, which could reduce the number of unplanned pregnancies and of unwanted children. I will confine myself to making one point. I believe that, since the world depression

began in 1929, the movements of birth-rates in Western countries have proved that, in an industrially organised, urbanised, and sexually sophisticated country, fluctuations in the standard of living are sensitively reflected by movements of birth-rates. In this respect developed countries differ from underdeveloped countries. When, during the world depression, unemployment was widespread and living standards fell, the birth-rates of many industrialised countries touched the lowest levels yet on record: indeed, fears were widely expressed of an impending depopulation of the West, if not of the whole world. (Whether the birth-rates were reduced by contraception or abortion is here immaterial.) But the tide turned in a way that few could have expected. Insecticides and antibiotics, by causing a fall in death-rates which was almost unimaginable in the middle 1930s, have resuscitated the Malthusian dilemma in a new 20th-century form. Since 1945, furthermore, there has been a remarkable wave of prosperity in the West which has kept birth-rates higher than most demographers thought probable ten years ago. If we have another depression, it is likely that birth-rates will slump as they did before. Many families in what I have called sexually sophisticated countries will then plan down their families to one or two children as they did thirty years ago. But the very-small-family system is not wholly beneficial to the child, who can suffer as much from being spoiled as from being neglected. The effects of spoiling, moreover, can reverberate through later generations no less than can the effects of neglect and cruelty.

Turning from genetic to educative measures, I believe that there exists within our reach a simple, practicable, and economical measure for improving family life—namely, seminars for primigravidæ. The argument is this.

There is no moment when the average woman is more receptive to guidance as to how to rear her children than when she is pregnant with her first child; and there is no moment when that guidance can be more effectively applied in the prevention of maladjustments and discords, seeing that the beneficiary is not yet born. The soil is at its readiest, and the moment for sowing the seed is the best. The lessons learned, moreover, stand the mother in good stead when she has more children.

I believe that certain elementary principles of pædiatric importance can be effectively inculcated in the course of such seminars. The leader of the seminar puts them forward for discussion, and invites each of the participants to comment on them in the light of her own experiences of childhood. The women taking part in the seminar have in common the impending crisis of first maternity, so that inhibitions and shyness quickly disappear. Indeed, an excellent basis is laid for enduring friendships within the group, the members of which sometimes continue to meet after their deliveries. They take an interest in each other's children, who may become playmates.

If services for maternity and child welfare exist, it is easy to form a group of from 8 to 12 primigravidæ who expect delivery within about a month of each other. The seminars can be held in any convenient premises. All that is needed is a room that is pleasantly furnished and a canteen which can provide something to eat and drink—an important requisite in all seminars. The premises of a maternity or child-welfare centre might be appropriate; or those of a pædiatric unit, a child-guidance unit, or an obstetric unit. More important than the location of the meeting-place is the personality of the person conducting the seminar. A married woman of professional status who has herself had children is well placed. It is advantageous for her to be a doctor, but in no way indispensable. The cost of arranging and holding such seminars is negligible.

What principles should be instilled into such a group? Each of us has his own ideas. My personal experience has led me to favour the five which follow, of which the first two are scarcely controversial:

1. When you are with the baby, be gentle and serene. Avoid showing fear, anxiety, or irritability, even if you have these feelings. Make the baby feel as safe as you can, and do not be afraid of showing affection or of letting its father show affection.

2. Never, if you can help it, leave the child for long in solitude (except at night) during its first three years, and try not to be separated from it for more than a few days. If separation is unavoidable, leave it in the care of someone it knows and with whom it feels safe.

3. Encourage the child at each stage of its growth to be as self-reliant as possible. Give it credit for as much trustworthiness, sense, and initiative as you can. Praise and reward it when it shows these qualities, and give it opportunities of displaying them.

4. Make for the child as few non-restrictive rules as possible in the light of its age. Explain these rules as they are made and also what punishment will be incurred if they are broken. If your rules are knowingly broken, punish the child as you said you would do. But use all forms of punishment sparingly. Steer a middle course between strictness and laxity; also between spoiling and neglect.

5. Discuss with your husband the rules you make and the form of discipline you will use as the child grows. When these are agreed between you, *back each other up*. Children can be clever in exploiting the more indulgent parent, often to the annoyance of the other.

These five precepts are simple and can form a basis for discussion at the seminar. Many additions will be suggested, and many views advanced, especially on the value of sex education and on the use and abuse of discipline. It is rather surprising how some women find these topics difficult to discuss with their husbands: these may suggest that husbands be invited to join the seminar. This arrangement can be successful. Many women will describe their own troubles in childhood. The seminar further offers an excellent opportunity to discuss other important matters, such as safety precautions in the home and the physical problems of child care. Most important from the standpoint of this conference, it provides the best possible occasion to give instruction on the spacing of children. The leader could ask how long the participants in the seminar want to wait before they have another baby and what birth-control methods they think are best. Eugenic problems, if they exist, can be discussed.

Some women, obviously, will refuse to attend such a seminar, and among them will be women who come from what we call " problem families ". These are notoriously difficult to reach and to influence. Some women will come but will be too stupid or too immature to benefit. Seminars for *primigravid* women, as here suggested, may have been tried in certain countries. If so, I do not know of them and I hope that I shall be told.

But I am far from supposing that seminars for primigravidæ are a panacea or cure-all. I merely claim that they could help many women and do much good for posterity. The families of the future would stand to benefit. The number of women involved would, at first, be small; but as the seminars (and their leaders) gained in reputation

and popularity, the numbers would increase. At the end of a vigorously executed ten-year plan, they might be attended by as many as two-thirds of the primigravid women living in the non-rural districts of a country like Britain.

I am indebted for useful criticisms of this paper to Prof. Aubrey Lewis, to Dr. J. P. M. Tizard, to Mrs. Joan Rettie, and to Dr. Margaret Neal-Edwards.

Public Health

ECHO TYPE-9 MENINGITIS IN EAST SCOTLAND

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IT is now recognised that the clinical syndrome of aseptic meningitis ("non-paralytic poliomyelitis") has often been caused by both poliomyelitis viruses and the group-B Coxsackie viruses. Recently an association has also been shown with two of the fourteen serological types of Echo (enteric cytopathogenic human orphan) virus so far identified. Cases of aseptic meningitis attributed to Echo virus type-6 were reported in the United States (Karzon et al. 1956, Davis and Melnick 1956), and outbreaks were recorded of a similar illness in Europe (Svedmyr et al. 1956, Johnsson et al. 1957). A similar illness caused by Echo virus type-9 has been reported in Europe (Tyrrell and Snell 1956, Boissard et al. 1957, Quersin-Thiry et al. 1957, and Nihoul et al. 1957), and in the United States (Sabin 1957).

We here describe the clinical and laboratory aspects of an outbreak of aseptic meningitis caused by Echo virus type-9 in East Scotland from July to November, 1956.

Epidemiology

32 patients were admitted to King's Cross Hospital, Dundee, with aseptic meningitis between July and November, 1956. Reports from general practitioners in the area indicated that many more patients were being dealt with at home. Of those admitted to hospital, 23 lived within the Dundee City boundary (population 178,946); 5 patients were admitted from Coupar Angus (population 2205) and 1 from the neighbouring village of Newtyle (population <1000). Towards the end of the outbreak 3 patients were admitted from the Perthshire village of Bankfoot (population <1000).

The homes of the Dundee patients were visited and in 9 families there was clear evidence of illness of a similar though usually milder nature; in a further 5 instances there was a similar illness in a contact outside the family circle. 4 of the 5 patients from Coupar Angus had contact infection, and from Bankfoot the 3 patients were a mother, daughter, and close family friend. In all, there were 4 instances where 2 members of family were admitted to hospital. The interval between dates of sickening in these lay between four and six days, and it is suggested that this is a probable incubation period.

The age- and sex-distribution is shown in table I. The series is small, but the attack-rates for males and females appeared about the same. Three-quarters of the patients were between the ages of 5 and 20 years.

* Sir Maurice Bloch Fellow in Virology.

TABLE I—AGE- AND SEX-DISTRIBUTION

Sex	Age (yr.)								
	0–2	2–4	5–9	10–14	15–19	20–24	25–29	30+	All ages
Male	2	4	4	3	4	0	0	0	17
Female	0	0	7	3	3	1	0	1	15
Total	2	4	11	6	7	1	0	1	32

Clinical Features

The main clinical features were:

	No. of cases		No. of cases
Pyrexia	30	Eye pain	6
Headache	29	Abdominal pain	3
Vomiting	28	Drowsiness	6
Neck stiffness—slight 9, —marked 18	27	Irritability	2
		Giddiness	3
Kernig's sign—slight 10, —marked 7	17	Nystagmus	1
		Rash	3
Muscle pain	9		

The onset was usually sudden. The average time between onset of symptoms and admission to hospital was four days (range one to ten days). A combination of pyrexia, headache, and vomiting, with signs of meningeal irritation, was the most common presenting syndrome. 9 patients had muscle pain which was always mild. Pain on moving the eyes was a very definite feature in a few patients in the older age-groups; there was no photophobia. A rash was present in only 3 cases—morbilliform in 1 and scarlatiniform in 2. Practically all patients were pyrexial on admission to hospital, temperature ranging between 100 and 102°F. The average duration of pyrexia from the onset of illness appeared to be between seven and eight days. An interesting feature was a tendency for the temperature to rise abruptly immediately before its final return to normal.

Most patients were ill for a few days but recovered quickly and completely. No complications, sequelæ, or relapses were observed.

Laboratory Findings

Cerebrospinal Fluid

Lumbar puncture was carried out on admission, and subsequently punctures were performed at about weekly intervals until the fluid was approaching normality.

Initially the cerebrospinal fluid was invariably under increased pressure, but usually the increase was slight and

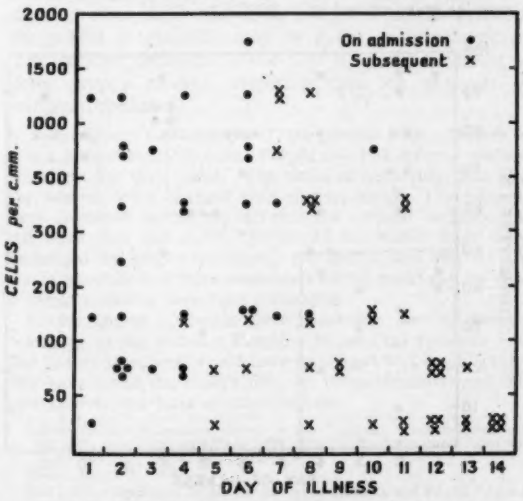

Fig. 1—Cell counts in cerebrospinal fluid.

certainly less than the average in pyogenic and tuberculous meningitis. The colour varied between clear and distinctly turbid. Many of the fluids were sufficiently turbid to have been confused with the appearances in bacterial meningitis.

The cell-counts varied greatly (fig. 1), and counts approaching 1500 per c.mm. were not uncommon even up to the sixth and eighth day of illness. In some cases cell-counts, initially low, tended to rise towards the end of the first week and sometimes this was associated with a worsening of the symptoms. Cerebrospinal fluid was usually normal or approaching normal by the fourteenth day.

Differential cell-counts were done on all fluids and the results related to day of illness are set out in fig. 2. During the first four days of illness there was an excess of polymorphs in 8 of 22 fluids examined. After the fourth day lymphocytes almost invariably predominated. There appeared to be no correlation between the cell-count and the nature of the cell, since an excess of polymorphs or lymphocytes was observed in both low and high counts. An observation of interest, if not of practical value, was the presence of rather unusual lymphocytes often in large numbers. These cells were large, stained poorly with methylene blue, and were rather " basket-cell-like " in appearance.

The protein content did not exceed 160 mg. per 100 ml., and in most cases it was less than 100 mg. There was no tendency for protein content to increase later in the illness, and if any cell-protein dissociation existed it was in the comparatively low protein contents often associated with high cell-counts. Sugar contents were within the normal range.

Erythrocyte-sedimentation Rate

The E.S.R. (Westergren) was noted in 19 patients. Results ranged between 1 and 32 mm. in the first hour.

White Count

In 28 patients examined, the count was less than 10,000 per c.mm. in 18, and in the remaining 10 it ranged between 10,000 and 15,000 per c.mm. Differential counts were either normal or showed an increase in polymorphs. No abnormal cells were found.

Virus Investigation

Materials and Methods

A stool and a sample of serum were collected from 24 patients on admission to hospital—i.e., at various intervals after the onset of illness. A second serum specimen was obtained about ten days after the first. Separated serum samples were stored at −20°C.

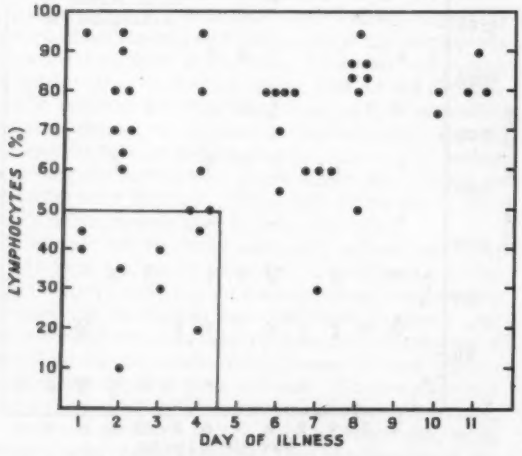

Fig. 2—Percentage of lymphocytes in C.S.F. cells.

TABLE II—RESULTS OF VIRUS ISOLATION AND SERUM-VIRUS NEUTRALISATION TESTS ON ACUTE- AND CONVALESCENT-PHASE SERA TESTED WITH ECHO VIRUS TYPES 6 AND 9

Case	Age (yr.)	Day of disease acute/ convalescent	Echo-6 antibody titre acute/ convalescent	Echo-9 antibody titre acute/ convalescent	Monkey-kidney tissue-culture of stool
1	3	5/15	•/<8	4/16	Negative
2	7	6/15	•/<8	<2/16	Negative
3	8	6/17	•/<8	<16/128	Echo 9
4	4	12/20	•/<8	<16/64	Echo 9
5	5	5/17	•/<8	<16/32	Negative
6	1	6/18	•/<8	<16/64	Negative
7	2	4/13	•/<8	8/16	Negative
8	10	7/19	•/<8	16/64	Negative
9	7	4/13	•/<8	<16/128	Negative
10	6	9/18	•/<8	<16/128	Negative
11	13	7/19	•/<8	<16/64	Negative
12	6	4/16	•/<8	16/32	Negative
13	3	4/16	•/<8	4/16	Negative
14	5	6/17	•/<8	<16/64	Negative
15	4	6/17	32/32	<16/128	Negative
16	17	9/20	•/<8	16/128	Negative
17	11	5/23	•/<8	8/8	Negative
18	34	2/21	•/<8	16/64	Echo 9
19	18	7/18	•/<8	<16/32	Negative
20	15	10/21	•/<8	16/>128	Negative
21	8	9/21	•/<8	<2/16	Echo 9
22	6	11/23	•/<8	4/16	Negative
23	2	11/26	•/<8	<16/32	Negative
24	0·3	9/27	•/<8	4/4	Echo 9

• Acute serum not tested.

Each stool was homogenised in phosphate-buffered saline to make a 10% suspension. This was centrifuged at 3000 r.p.m. for thirty minutes and to the clear supernate were added penicillin and streptomycin to a concentration of 100 units and 0·1 mg. per ml. respectively. The fluid was then stored at −40°C.

Virus isolations were attempted both in HeLa cells and in trypsinised monkey-kidney cultures prepared according to the method of Bodian (1956). The cells were grown and maintained in Hank's solution with 0·5% lactalbumin hydrolysate and 2% inactivated calf-serum added. 0·1 ml. of the stool extract material was inoculated into each of 3 tubes of HeLa and monkey-kidney cells, and the tubes, which were incubated at 37°C, were examined daily for cytopathogenic changes. Three serial passages were made before a specimen was considered negative in either tissue. When cytopathogenic changes were observed, 0·1 ml. of tissue-culture fluid was mixed with an equal volume of 1/8 dilution of antiserum, prepared in rabbits, to Echo virus types 6 and 9. The serum/virus mixtures were inoculated into monkey kidney-cell cultures, which were observed for neutralisation of cytopathogenic effect by homologous antiserum.

Antibody contents were determined in monkey kidney-cell cultures, with an Echo type-9 virus (719) isolated from 1 patient. For purposes of comparison a prototype strain of Echo 9 (Hill) and of Echo 6 (D'Amori) were also used. Appropriate dilutions of serum, previously inactivated at 56°C for thirty minutes, were mixed with equal quantities of virus containing 40–50 tissue culture infective doses (T.C.D.$_{50}$). The serum/virus mixtures were incubated at room temperature for an hour and were then inoculated into duplicate cultures of monkey-kidney cells. Tests were read when the virus controls showed complete degeneration, usually at the fourth day. Absence of cytopathogenic effect was accepted as evidence of neutralisation. The reciprocal of the highest initial dilution of serum producing neutralisation is recorded as the end-point of the titrations.

Results

Virus isolations.—Cytopathogenic agents were isolated from 5 stool specimens in monkey-kidney cells, whereas none was recovered in HeLa cells. All the agents were neutralised by antiserum prepared against Echo virus type-9 and none by Echo-6 antiserum. Antiserum prepared against each of the 5 agents in rabbits exhibited reciprocal neutralisation with the homologous virus and the other 4 agents. Each antiserum neutralised the prototype Echo-9 (Hill) strain. Each virus was inoculated by the intraperitoneal route into suckling mice but no paralysis was observed.

Serological results.—The results of neutralisation-tests with Echo virus types 6 and 9 on acute-phase and

convalescent-phase serum from the 24 patients studied are correlated in table II with the results of virus isolation.

A similar antibody titre was observed in each serum tested with the locally isolated strain of Echo 9 and with the prototype virus. A fourfold or greater rise in antibody titre to Echo 9 was observed in 20 instances; in 2 a twofold rise was observed and no significant antibody was found in the remaining 2 cases. From 4 patients who showed a fourfold rise in homologous-antibody titre, Echo virus type-9 was isolated, but the fifth isolation was from a patient in whom no increase in an initially very low level of antibody was found by the twenty-seventh day of illness. 1 patient, whose stool yielded no virus and who produced a diagnostic rise in antibody to Echo virus 9, also had a neutralising-antibody titre of 32 to Echo virus 6 in both acute and convalescent serum specimens, suggesting residual antibody after previous infection with Echo virus 6.

Comment

In the clinical diagnosis of aseptic meningitis due to Echo virus type-9 our findings suggest that 3 characteristics are of importance.

(1) There is often a familial association between cases, or evidence from the case-history of contact with the disease.

(2) The initial severity of the illness is in contrast with the subsequently benign course in all our cases.

(3) The various abnormalities in the cerebrospinal fluid, even in some cases with an initial predominantly polymorph response, return fairly rapidly to normal.

Although the number of viruses isolated was small they all appeared to be antigenically homogeneous. The rising antibody titres to Echo virus type-9 in 22 of 24 patients, together with the absence of poliovirus from the stools, provides further proof of the similarity of the infecting agent in each member of the group of patients.

Summary

32 persons with aseptic meningitis were admitted to hospital in East Scotland between July and November, 1956. 5 viruses belonging to Echo virus type-9 were isolated from the stools of 24 patients. Rising titres of antibody to Echo virus type-9 were observed in 22 of the 24 patients examined.

We are grateful to Dr. Mary Proudfoot, assistant medical officer of health, Dundee, for her help in investigating illness among contacts of patients; to Dr. A. D. Macrae, Virus Reference Laboratory, Colindale, for supplies of seed virus; and to Mr. H. G. Carson, F.I.M.L.T., and Mr. J. Kerr for technical assistance.

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New Arrangements for B.C.G. Vaccination

The Ministry of Health has issued a revised version of its memorandum [1] on B.C.G. vaccination. Besides the Danish liquid vaccine used hitherto, the British freeze-dried vaccine will now be introduced, and for the nine months beginning April 1, local authorities may use either type; the position will then be reviewed. The liquid vaccine will continue to be supplied as at present through the Public Health Laboratory Service, but the freeze-dried vaccine will be supplied direct by Glaxo Laboratories. Diluent will be supplied to local authorities. Orders should be placed, as before, through the Ministry of Health, Savile Row, London, W.1 (in Scotland, through the Infusion Fluids Laboratory, 112, Ingram Street, Glasgow, C.1). Vaccine is still available only to hospital and local-health authorities; eligible hospital workers include not only nurses and medical students but anyone at special risk from patients or fomites.

1. 322/B.C.G.; see *Lancet*, 1953, ii, 1049.

Plastics in Food Packaging

When the incidence of food-poisoning is high, the attraction of ready-packed food increases. Many plastic materials suggest themselves for packaging, for they can not only be clean but also be seen to be clean, and their poor chemical reactivity makes toxicity unlikely. But, though no ill effects have been reported, the plastics industry was concerned lest some material used in processing the plastics might be toxic; and a committee appointed by the industry has suggested a basis for a voluntary standard of performance of plastics[1]; maintenance of this standard would exclude a plastic for use with food if it presented any toxic hazard.

Medicine and the Law

Duty to Provide Medical Care

THE duty of parents to provide adequate medical attention for children has been emphasised in a warning given by Mr. Justice Paull to a couple charged with the manslaughter of their newborn baby.[2]

The couple were Jehovah's Witnesses and had refused a blood-transfusion to the baby—apparently on religious grounds. The case ended suddenly after the family doctor had said in evidence that he had not warned the parents that failure to give a transfusion would cause the child's death. He remembered telling the father that the child should go into hospital for a transfusion, but he could not recall speaking of death.

The judge then stopped the case, but told the parents: "If after all that you have learned in this court anything like this happens again, the position may be quite different. Just remember that."

There can be little doubt that the judge's warning was fully justified, having regard to the existing law. It has for many years been a statutory offence [3] to cause unnecessary suffering to a child by wilful neglect, and the decided cases show that if such neglect results in death the parent or guardian may be guilty of manslaughter. The decided cases also show that it is wilful neglect to deny proper medical attention even on grounds of religious objection.

In the Queen *v.* Morby (1881) the parents were members of a sect known as the Peculiar People and had refused medical treatment for their child. The child subsequently died and the parents were charged with manslaughter. The parents were acquitted on the ground that the medical evidence did not show that the child's life would necessarily have been prolonged by proper treatment; the doctor said that its life would possibly have been prolonged but he could not say that it would probably have been prolonged.

In the Queen *v.* Senior (1899)—another case of parents belonging to the Peculiar People—the medical evidence was that proper treatment would have prolonged and would probably have saved the child's life. In those circumstances the parents were convicted of manslaughter.

1. British Plastics Federation: report of the "toxicity" subcommittee of the main technical committee. 1958. Pp. 20. 5*s*. Obtainable from the Federation, 47, Piccadilly, London, W.1.
2. *Times*, March 1, 1958.
3. The current legislation on this subject is the Children and Young Persons Act, 1933.

In England Now

A Running Commentary by Peripatetic Correspondents

THE high spot of our last clinical meeting was the Brains Trust—five patients on the platform with a doctor in the chair and an unleavened medical audience. The patients were all experienced victims of hypotensive medical therapy (grateful victims, let it be said; for three had presented with retinal hæmorrhage and the other two with cardiac failure). They were soberly authoritative on the merits and demerits of the various drugs, and each had his own way of regulating their side-effects. One panellist, a business executive, had become an expert on constipation (senna pods and molasses for him, and a rule that he did not take his morning hypotensive dose until after evacuation). Another, technical director of a large organisation, had sublimated his skills to the taking of his own blood-pressure (he thought his readings could bear comparison with those of the average nurse). A schoolmaster was coping successfully with the twin snags of treatment and the hypertensile effect of prolonged dealings with the young. The other members, from being bedridden, had returned to the harassing task of running an hotel and to a job as an industrial foreman.

They agreed that it took about eighteen months to adjust to treatment and to learn to live with the disease. They laid stress on the problem, to hitherto energetic men, of episodes of depression and of the frustrating languor experienced at times when the blood-pressure had become too low. To begin with they had all found a dry mouth troublesome, but this had lessened with time, and they were not favourably impressed by drugs to counteract side-effects. They rattled off preparations and dosages with an easy familiarity which emphasised the pharmacological shortcomings of at least one member of the audience.

Another member, in thanking the panellists, expressed wonder and not a little envy at the chairman's good fortune in acquiring them. He had not realised that such intelligent patients existed.

* * *

The old grey Social Worker leant forward : " He's a good boy, you know," he pleaded : " of course I know there's a lot against him, but he thinks a lot of his old Mum and I'd like to carry on and see if there isn't something more I can do for them." He had come half across London to talk about the lad before I wrote the psychiatric report. There was indeed a lot against him : a string of convictions as long as your arm, child-guidance failure, probation failure, approved-school failure, and now the shadow of borstal was lengthening across his path. I knew (though he'd never admit it) that the old man had far too many cases to follow up, and most of them from hard-core problem families whose hides were as leather against the patient permeations of the social services. Yet he was proposing to give up more of his rare evenings by the fireside for another thankless (and one feared useless) attempt to salvage this boy. There must be a reason for his persistence ; he was *involved*, that was it. He had allowed his parental instincts to escape control ; he had lost objectivity and his reality-testing had gone for a Burton. Why, he might even lend the lad money !

It all called to mind the attitude of two symbolic friends of mine. One was a young American surgeon of deep Christian convictions who told me with tears in his eyes : " When my patients are sick, believe me I suffer every pang with them," and the results of his major surgery in the ghastly climate of the full monsoon were impressive testimony to the value of his prayers. My other friend couldn't face this approach ; he had fled to the impersonal comforts of the test-tube and microscope : " You must know your cases only as numbers and consider each problem in vacuo as an academic one : otherwise you die young."

As my emotional state moves me up and down between these two extremes, I ponder on what I should really feel about my patients—are they friends, acquaintances, or merely a source of income ? Is the professional relationship an all-excluding one or can I join my patient in the Saloon Bar after psychotherapy, or get him to help me paint the garage doors ? Should I ring up my pals when he's out of a job or send him down to the D.R.O. ? If he's difficult about appointments or rude, do I give him hell and forget him, or try to meet him more than half way ? If one of my depressed spinsters gives me as a parting gift a small embroidered (O.T.) traycloth, do I politely hand it back and mutter about hospital rules ? Or what if she gives me a crate of whisky ?

I suppose, like the old man, I love my patients really, or most of them ; perhaps I should get someone to analyse my counter-transference. But my love is as nothing compared to his—bless him. The report was sent, the court was lenient, he's got his case, and good luck to him : I'm afraid he'll need it.

* * *

I blame furnaces. When I was young I'd come 'ome an' take off me vest an' stand it up on t' floor—stiff wi' sweat.

Now then, Doctor doesn't need to know thee pedigree!

Thee pipe down, lass. *I'm* tellin' doctor what 'e 'as to know to make a guess at me condition. An' I suffered then from t' same symbols as I suffer from now. When I pass me wind . . .

Why bring that up ? Doctor can't better thee manners.

Me manners ? What's it to do wi' me manners ? When I feel as summat lies dead in me stummick an' embrocation 'as set in—is that me manners ?

Nay lad, but I'll tell thee what it is an' I'll tell doctor what it is—it's beer . . . bottles and barrels of it lyin' flat an' bleak in thee belly, an' it'll save Doctor time if tha told 'im so . . .

Careful, lass!

Where was thee Friday night ? An' Saturday an' Sunday too ? Soakin' it up at t' Oak till it were runnin' out of thee lugs an' breakin' into gas; an' thee trumpetin' through t' night an' waken up in t' mornin' like a shovel-load of cinders in a pot of porridge!

Thou 't in 'igh glee this day, lass. Has t' ever thought of joinin' Missions ? She gets like this, doctor. 'Er sister Maggie goes round pubs wi' War Cries . . .

Only place to get at chaps like thee . . .

Well, it's 'er only 'ope of gettin' clear of that weak, simperin' tee-totlin' drip of a man of 'ers . . .

* * *

My student days were spent commuting from the middle suburbs to Gower Street. By leaving home at 8.14 A.M. I could just make the 9 A.M. lecture. For Thursdays we had the surgeon's firm promise that he would never start before 9.10 A.M. This allowed time for an extra slice of toast. A readership poll of my travelling companions of those days showed:

50%	*Daily Telegraph.*
20%	*Express.*
20%	*Mail.*
0·2%	*Lancet.*

If I was very late I would travel with those who are now known as " Top People ", or even with *Financial Times* readers. Oh, thought I, for the days ahead when as a G.P. I shall be on the job, with no travelling, reading the journals in a fireside peace, away from strap-hanging.

These reminiscences were prompted by the clock reading of 10,000 miles which appeared this week on my six-month-old car. Even allowing for my wife's shopping, and some fast driving over the straighter roads, this works out at about $1^1/_2$ hours daily at the wheel. A car radio, of course, is one way of making this time more productive, but it can be frustrating, for you tend to arrive at a patient's door just before the climax of a play and emerge in time for the cast list. The end result is that you spend more time than ever in the car. Perhaps a portable tape playback is a better answer ? We may then look forward to a major metamorphosis of *The Lancet* [1]—its imago form as a spool of tape.

* * *

Prof. Raymond Dart, of Johannesburg, who has just been awarded the Viking medal by the Wenner-Bren Foundation of New York for his work on human origins, is the author of a paper entitled the *Makapansgat Australopithecine Osteodontokeratic Culture.*

Professor Dart is emphatic
That Australopithecine " man "
Was osteodontokeratic,
And that is how Man began!

1. *Lancet*, Jan. 4, 1958, p. 38.

Letters to the Editor

BUDGERIGARS AND POLIOMYELITIS

SIR,—Dr. Sommerville and his colleagues (March 8, p. 512) reported an association between a fatal case of bulbar poliomyelitis and a budgerigar which was excreting type-1 poliovirus. The only other reference we know to the circumstantial association of a sick parakeet and poliomyelitis appears in a paper by Fox and Chamberlain.[1] In this instance there were four fatal cases of poliomyelitis in one household, but no virus was recovered from the bird.

Last week's report has naturally caused anxiety to people owning pet budgerigars, and we feel that a preliminary communication about our studies on the susceptibility of these birds to human polioviruses may be of some interest.

A Belfast strain of type-1 poliovirus isolated from the fæces of a paralysed child in 1957 was used for budgerigar inoculation experiments. Monkey-kidney tissue-culture (M.K.T.C.) passage virus was first titrated in M.K.T.C. and then used for the intracerebral inoculation of rhesus monkeys and for the inoculation of budgerigars. The paralysing dose$_{50}$ for monkeys was equivalent to $10^{3\cdot8}$ tissue-culture doses$_{50}$ (T.C.D.$_{50}$) of virus, three monkeys being used for each log dilution of virus. Three budgerigars were inoculated intracerebrally with $10^{4\cdot5}$ T.C.D.$_{50}$ of virus, and four budgerigars were inoculated orally with $10^{5\cdot2}$ T.C.D.$_{50}$ of virus. Three more budgerigars were kept as cage contacts of orally inoculated birds. One orally inoculated bird died suddenly on the 5th day: this death was considered to be non-specific, as no virus could be recovered from the brain or intestine and contents. The other birds remained healthy for 4 weeks. Fresh fæcal specimens were collected from all birds for 19 days after inoculation and tested for the presence of poliovirus. None of the birds excreted detectable amounts of virus during this period. Serum taken on the 26th day from each bird was tested in M.K.T.C. at a 1 in 10 dilution for neutralising antibody against each of the three types of human poliovirus. Approximately 100 T.C.D.$_{50}$ of virus was used for these tests. No antibody to any of the three poliovirus types was found in the serum of any bird.

We consider that our failure to infect budgerigars with a virulent type-1 poliovirus gives hope that the natural infection of these birds may prove to be a rare event.

G. W. A. DICK
D. S. DANE.

Department of Microbiology, Queen's University, Belfast.

SIR,—The preliminary communication by Dr. Sommerville and his colleagues was most interesting. The numerous instances of recurrent cases of poliomyelitis at long intervals in relatively rural areas can be explained only by long-term carriers, but I am convinced that these are more probably human than bird or animal.

I wonder whether, in this instance, the carrier state of the rest of the human household is known? It is only an assumption that the original illness of the budgerigar was caused by poliomyelitis virus. An alternative assumption is that some other infecting organism was concerned, the bird subsequently being infected with poliomyelitis virus by a human and acting as a mechanical excreter of virus fed to it from this human source. I cannot help wishing that the bird had not been destroyed on Oct. 7; it would have been interesting to see how long the carrier state continued.

E. R. HARGREAVES.

Mawnan, near Falmouth, Cornwall.

1. Fox, M. J., Chamberlain, J. *J. Amer. med. Ass.* 1953, **151**, 1099.

THE MISUSE OF THE TOURNIQUET

SIR,—In the right circumstances a tourniquet is a useful, helpful, even indispensable aid to operating. Its use can transform a difficult intricate dissection into a procedure of great simplicity; but it is nevertheless repugnant to the physiologically minded surgeon.

It has become customary to use a tourniquet in almost all limb operations, and particularly in the treatment of fractures and the repair of nerve injuries. Such a routine is harmful and a backward step in the advance of surgery. I hear of tourniquets being left in place, it is said without harm, for two hours or more; even three hours have been mentioned to me. This is running two unjustifiable risks: the long interruption of the circulation may cause injury to nerves and muscles; the metabolism of the tissues may be so damaged (though the tissues are capable of eventual recovery) that, for a time, the power of immune response is in abeyance and infection follows. I am convinced that this is an important factor in the far too common onset of infection after complicated limb dissections. Enormous œdema occurs when the tourniquet is removed, and lasts for a number of days. During this time the lymph stagnates in the distended tissue spaces. The conditions are ideal for the growth of those bacteria which inevitably fall into every surgical wound however stringent the aseptic precautions taken are.

It will be said that with a tourniquet applied the operation is not only much easier but much safer and quicker. Easier and quicker it may be, but it is not safer for the patient. I began my active surgical work in the Arbuthnot Lane era. No surgeon at this time ever thought of using a tourniquet when plating a fracture, even the most complicated. In the 1914–18 war thousands of nerve sutures were performed without its use. I was trained to remove cartilages from the knee without a tourniquet. Then for a period I operated with one. The postoperative swelling, pain, and increased time needed for recovery were so much greater that I reverted to operating without a tourniquet—but, of course, without the legs dangling over the edge of the table, the customary position, which causes congestion.

Tourniquets are not used in the abdomen, in the neck, or within the head. In many other places their use is impossible. The brachial plexus, for example, must be displayed without one. Why, in the case of the limbs, is there this forgetfulness of the vital processes which go on within living cells and their necessary preservation if quick and sound repair is to take place?

Let me add that in some circumstances a tourniquet is almost indispensable—namely, in such operations as the removal of the palmar fascia for Dupuytren's contracture, to protect the digital nerves, and for the repair of cut digital nerves themselves. In any case the very longest time a tourniquet, even a distended windbag, should be left in place is one hour; and ideally that is one hour too long.

CHARLES A. PANNETT.

Basingstoke.

TREATMENT OF UNDULANT FEVER

SIR,—I have read with great interest Dr. Torres Gost's article (Jan. 25). I regret that I cannot share his enthusiasm or his firm conviction that novobiocin ('Cathomycin') is the ideal antibiotic in the treatment of brucellosis.

In 1955 I had the opportunity of using this antibiotic through the courtesy of Prof. W. Spink, who was then on a visit to Malta. Subsequently I received a generous supply from its makers. The original intention was to treat 50 cases, but the

experiment had to be stopped at 22. With a dosage of 1·5 g. daily the results were not so constant or dramatic as those with tetracycline. When 2 g. was used the same results were obtained—that is, rapid defervescence and improvement in three to four days—but in 7 cases, exactly on the seventh day, there was a severe urticarial rash with rise in temperature and sometimes headache and vomiting. I am afraid that my patients were not of such a Spartan cast as those of Dr. Torres Gost, and treatment had to be stopped.

In the 15 patients who completed a fifteen-day treatment, there were 5 relapses (bacteriological) within four months, which is roughly our figure when tetracycline is used. In the 7 patients who did not complete the course there were 4 relapses within two months.

I was brought up in an old school, and my aim has always been to treat patients *tuto, cito, jucunde*. I will not go so far as to say that novobiocin is dangerous, but the rash and the fever do not add to the *jucunditas* of the patient. It has no advantages over the tetracyclines, and in my opinion its usefulness lies in another sphere—in the treatment of staphylococcal pneumonia and of bronchiectasis, where the results are really marvellous.

After the generosity of the makers of novobiocin, I feel somewhat reluctant to write this letter. I can justify my action, to myself, only by another Latin tag—*amicus Cæsar sed magis amica veritas*.

St. Luke's Hospital,
Valletta, Malta. J. E. DEBONO.

ÆTIOLOGY OF PRE-ECLAMPTIC TOXÆMIA AND ECLAMPSIA

SIR,—Does Dr. Schuurmans (March 8) consider that "it is highly probable that the increased frequency of toxæmia of pregnancy and pre-eclampsia in patients with beri-beri" (in whom he states the adrenals are hyperplastic) "and pellagra" (in whom he infers that the adrenals are atrophic) "must be ascribed to the adrenals too"? Is it possible that both excess and deficiency of adrenal secretion equally provoke toxæmia?

London, W.1. JOHN SOPHIAN.

ILEOSTOMY CHEMISTRY

SIR,—You refer to our work on electrolyte losses from an ileostomy stoma in your annotation of March 8. Dr. Abbott and his colleagues, in a letter last year,[1] questioned the high levels of sodium output we obtained in the immediate postoperative period (approximately 300 mEq. per litre). As you have observed, it is difficult to understand how such a high concentration can occur; we think that we now have an explanation.

We checked the methods we had employed [2] against duplicate estimations undertaken in another laboratory. The results always tallied. Since no error could be found in technique we considered once more sodium intake, more particularly since estimations undertaken in more recent cases have only occasionally revealed the high output we observed at the beginning of our investigations some four years ago. The methods of administering sodium and the quantities given had not substantially altered. Inquiry revealed, however, that the source of supply of salt tablets was changed by the dispensary about two years ago because of complaints that they appeared undigested in the normal stools of other patients to whom they had been administered. Our patients receive additional salt by mouth as soon as the ileostomy begins to function, in two forms—by "enteric-coated" capsules prepared in the hospital dispensary and by tablets supplied by a pharmaceutical company which also have some form of "enteric" coating. We have observed neither in undigested form at any time in the 24-hour collections from which aliquots were taken for our estimations. It is quite possible, however, that such tablets passed with the ileostomy excreta in semi-digested form, then dissolved in the cans during the 24-hour collection period or perhaps when the contents were mixed prior to sampling, thus increasing the sodium concentration.

This seems to us to be the probable explanation, though we have not as yet been able to reproduce our earlier findings by administration of the offending tablets. Nor can we explain why, if our hypothesis is correct, the tablets have failed to dissolve properly in the intestines immediately following the institution of an ileostomy but have dissolved subsequently, and, furthermore, have done so following subsequent operations when they were administered, as before, and the sodium concentration has never been elevated above 150 mEq. per litre.

Queen Elizabeth Hospital,
Birmingham. N. CRAWFORD
B. N. BROOKE.

1. Abbott, W. E., Levey, S., Krieger, H. *Lancet*, 1957, ii, 149.
2. *ibid.* 1957, i, 864.

THE LIFE FOR ME

SIR,—One of the virtues of Dr. Richard Cobbleigh's Widdicombe letters is their briskness. My attempt to emulate it has led him (March 8) to misunderstand my use of his own term: "those Clinics". I used it about maternity and child-welfare centres in the sense he did about twelve months ago, when reflecting in an earlier letter on his not very extensive experience of them. Of course, any good G.P. can do this work—a good many in London in fact help us by doing it. But that in no way disproves the functional value of the M. & C.W. centre as such. As a medium for health education, as a forum for a mild gossip, as a convenient place to get food for the baby, as a means of giving a mother some feeling of security about her offspring, and as a convenient building for various prophylactic injections, it has uses most of which escaped Dr. R. Cobbleigh. Nor is it more likely to be a source of infection than a doctor's surgery.

But this is old stuff. London, like other local authorities, is now feeling its way (I think the phrase is reasonably accurate) towards the contribution it can make to preventive mental health. Any doctor or health visitor, knowing of a family with a problem in which there is a psychological or psychiatric aspect, can seek guidance at a case conference in the centre presided over by a psychiatrist. The field worker presents the case. The psychiatrist can (*a*) ask for more facts which the field worker proceeds to get, (*b*) indicate lines of approach to the family which may solve or ameliorate the problem, or (*c*) recommend reference to a specialist.

This is slow work. Though we have such conferences available in each of our nine health divisions we are finding that the field workers need about two years' regular attendance at these meetings before they are reasonably competent both to act on their own and to know when the problem is beyond them. But the system shows signs of justifying itself and as one lot of field workers graduates, so to speak, we hope to spread the training to others. To the psychiatrists who are helping us (paid for by the regional hospital boards) we owe a great debt.

The preventive value of a child-guidance clinic is another and much more complex matter. No-one has yet evolved a method of evaluating it; any such method would clearly involve observation over a period of years. But no clinic can succeed unless it works at least as much

with and on the parents as with the child. The importance of the preventive work we are essaying (quite apart from man-power considerations) is indicated by the fact that about 80% of the children referred to L.C.C. child-guidance clinics, at whatever age they come, are so referred because of difficulties which originated before the child was five years old.

J. A. SCOTT
Medical Officer of Health for the County of London.
Public Health Department, London, S.E.1.

EXPOSURE ON MOUNTAINS

SIR,—Exposure in mountaineers usually involves physical exhaustion as well as exposure to cold. On high Scottish hills it is often unpredictably cold, and the damp atmosphere further intensifies cold effects. Fierce winds may also contribute to conditions more conducive to hypothermia and exhaustion than those encountered at higher altitudes elsewhere in the world.

Severe physical effort leads to anoxia, and the combination of anoxia and extreme cold may induce ventricular filbrillation. This fatal event may ensue very quickly when the body is exhausted as well as cold; the idea that under such circumstances death is slow is erroneous, and so is the commonly accepted advice to keep moving at all costs. Those benighted on high hills in winter must strictly conserve their energy and find shelter, or at least some kind of wind-break, till conditions improve. One has safely lain out at heights over 3000 feet on hard winter nights, wearing only ordinary climbing clothing, while waiting for dawn to get casualties down. It is safe if one is not exhausted.

Often in mountain tragedies women have survived when men under similar strain have succumbed. I feel certain that women have the tougher constitution for this sort of ordeal; but it is hard for a male-ruled world to accept this, and women survivors have more than once been accused of causing the death of a male companion. A woman's power of endurance is illustrated by an accident in which four men died but a girl of comparable physique, with normal subcutaneous fat and similarly clothed, survived.

With four very fit men, one of whom was her husband, she had to struggle against a gale, said to reach 100 m.p.h., for 3-4 miles down a gently sloping snow-covered valley in Inverness-shire. One of the men began to tire; the girl and her husband supported him, following in the track of the other two who went ahead: it was nearly impossible to look up into the gale. Then they changed places, the other two supporting the weak one. A few minutes later the girl looked back at the three behind, and the weak one was not there; the others said, "He was out so we left him." Later she wrote: "I couldn't have had much feeling left, because I merely said 'Oh' and continued walking as if it were an everyday occurrence to leave one's friends lying in the snow in a deserted glen."

Then two of the men began to lag behind. "All three of the boys' eyes were glassy looking, bloodshot and unable to focus properly. They kept asking me if I was all right and would I make it. I never doubted that we would all make it . . . I said it was about a quarter of a mile to the bridge, although it turned out to be nearer a mile." One asked her how many steps there were in a quarter of a mile: "It was then I realised the boys were more exhausted than me."

Soon the men could not walk against the wind: "I kept lifting up the boys as they fell, and no sooner had I one up than the other would fall . . . I dragged them into a wee gully where the wind was slightly less strong. I tried to keep them warm and awake, and I fed them on chocolate and sweets. They fell asleep in about ten minutes after getting into the gully . . . It took us about half an hour to cover the last 30 to 40 yards during which the boys began to lose their senses. They stopped breathing about twenty minutes after they fell asleep. . . . The boys most definitely were not in pain and their death was quick and peaceful. I think their senses were numbed and they just fell asleep and died quietly. They didn't even seem to feel the cold and I know I didn't in spite of being soaked to the skin and lying in the snow. Although they lost their senses of sight and feeling, they definitely could still hear, because, in the gully, I chatted to the boys and my husband smiled when I spoke, although he just looked straight ahead and didn't say anything . . . I did not feel the wind as much as the boys and I have found that before." She struggled to a house and, after a wash and a hot drink, quickly recovered. She suffered no ill effects, but the four men died.

It is hard to explain this female superiority, shown too in a recent Channel-swimming success. Have they a better adrenocortical reserve, necessarily conditioned by the emergencies of childbearing? Conceivably male explorers, liable to exhaustion and exposure, should carry cortical extract for emergency use.

D. G. DUFF.
Belford Hospital, Fort William, Scotland.

THE DOCTOR'S ATTITUDE TO HIS PATIENT

SIR,—I read with interest, and growing surprise, Dr. Ryle's letter (March 1) about Dr. Clyne's article of Feb. 1. In the last sentence he administers the final blow by calling Dr. Clyne's approach "unscientific". Now Dr. Ryle is himself a family doctor and a very good one, and he should know that the emotional forces which operate within the doctor–patient relationship are as real, and as potent for good or ill, as any physical agent. Of course the disease must be described and investigated; that is part of the doctor's job, and it must be done thoroughly. The other part is the understanding and management of a personal relationship, and the "charges" of feeling that exist there. These, too, need to be described and investigated—objectively and in detail, as Dr. Clyne has done. They cannot be measured, as yet, but they can be studied—this is the first phase of any scientific inquiry. I think there is no doubt at all that more study of, and more teaching of the student about, what goes on between doctor and patient will in the end yield great benefits for everyone concerned.

DESMOND O'NEILL.
London, W.1.

INTRAGLOSSAL INJECTIONS: A COMPLICATION

SIR,—In his letter of Feb. 8, Dr. Robertshaw described a patient who, three days after receiving an intraglossal injection of suxamethonium, had pain and swelling of the tongue and cervical adenitis, which subsided with penicillin therapy. This picture suggests bacterial infection. The pain and swelling following chemical irritants injected intramuscularly is noticed within twenty-four hours, and usually begins to disappear in three days (e.g., chlorpromazine).

I have had no such complaint in five years of this practice, and I have personally followed up ten patients who, since Feb. 8, have received 100 mg. suxamethonium intraglossally. None of these patients made any spontaneous complaint: none had pain or swelling of the tongue. The only positive finding was aching and stiffness in the neck muscles for two days in two patients, attributable to the intraglossal suxamethonium; this was mild, and the incidence is similar to Hegarty's figure [1] for intravenous suxamethonium.

JOHN BULLOUGH.
Chislehurst, Kent.

1. Hegarty, P. *Brit. J. Anæsth.* 1956, **28**, 209.

BONE-MARROW DEPRESSION FOLLOWING TREATMENT OF TETANUS WITH PROTRACTED NITROUS-OXIDE ANÆSTHESIA

SIR,—In cases of tetanus treated by curarisation and artificial respiration, Lassen and his colleagues [1] presented evidence to suggest that bone-marrow depression was due to commercial nitrous oxide used for prolonged sedation. We report a further case which supports this conclusion.

A shearer and rabbit-trapper, aged 57, was admitted to the Royal Adelaide Hospital on July 7, 1957. Fourteen days previously he had cut the pulp of the ring finger of his right hand. Four hours after he reached hospital and forty hours after he first complained of backache and difficulty in opening his mouth, he had a generalised severe tetanic spasm. The terminal segment of the infected finger was amputated, under local anæsthesia, after 300,000 units of antitetanic serum had been administered. Next morning, difficulty in coughing and swallowing made tracheotomy necessary.

Six hours after tracheotomy, though sedation had been carried to the stage of "periodic" breathing, he still had tetanic spasms in response to stimuli, and it was decided to give tubocurarine and to begin artificial respiration using a respirator with positive and negative pressure phases. A mixture of 50% oxygen and 50% nitrous oxide was administered for continuous sedation through the carbon-dioxide absorber unit of an anæsthetic machine.

Before curarisation the patient was given: penicillin, streptomycin, mepyramine maleate, chlorpromazine, and paraldehyde, and mephenesin and promethazine by intermittent intravenous drip. Of these, only penicillin and streptomycin were continued.

On admission the hæmoglobin was 15 g. per 100 ml., and the leucocyte-count 18,300 per c.mm., of which 90% were neutrophils. Daily examinations thereafter revealed a progressive fall, and on the fifth day the leucocyte-count was 5200 per c.mm., of which 86% were neutrophils. At this juncture nitrous oxide was stopped, and the gas mixture was changed to (approximately) air 60% and oxygen 40%, with oral chloral hydrate and paraldehyde as basal sedatives.

On the sixth day, the leucocyte-count had fallen to 3500 per c.mm. with 28% neutrophils, showing an Arneth shift to the right. On the seventh day the hæmoglobin was 13.9 g. per 100 ml., reticulocytes less than 0.1%, platelets 230,000 per c.mm., and leucocytes 3600 per c.mm., with polymorphs 27%, lymphocytes 48%, monocytes 10%, eosinophils 4%, and plasma cells 11%.

During the succeeding days, the white-cell count rose rapidly to normal levels, which were maintained, but the hæmoglobin fell to 11.3 g. per 100 ml. on the eleventh day. Tubocurarine was stopped on the fifteenth day, and the tracheostomy tube was removed five days later.

Leucopenia, anæmia or thrombocytopenia have been previously described in 9 patients with tetanus treated by curarisation and artificial respiration; and all except 1 [2] had been given long-continued nitrous-oxide anæsthesia.

Lassen [1] first attributed this bone-marrow depression to commercial nitrous oxide, and his suggestion was supported by Wilson et al.[3] In our case the leucocyte-count began to fall on the third day, but the depression was greatest on the fifth and sixth days after beginning nitrous oxide; this corresponds with the interval recorded by Lassen, by Wilson et al.,[3] and by Last and Nicholas.[4]

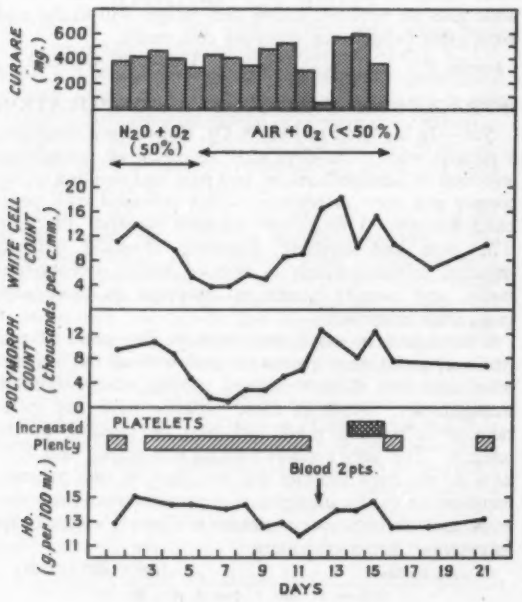
A number of other drugs have been common to the reported cases, including antitetanic serum, tubocurarine, and penicillin, but we feel that the improvement which followed the cessation of nitrous-oxide administration is strong evidence that this, or a contained impurity, was the toxic agent, particularly since no change was made in the other drugs being given at this time.

A high oxygen-tension has been shown to affect hæmatopoiesis,[5] but the bone-marrow apparently has not been depressed despite extensive use of 50% oxygen and 50% nitrogen mixtures in respiratory units for bulbar poliomyelitis, and it seems unlikely that the relatively small change in the proportion of oxygen in the inspired gases in this case could cause and reverse changes of such magnitude.

We wish to thank Dr. C. B. Sangster and Dr. R. A. A. Pellew, under whose care this patient was admitted to the Royal Adelaide Hospital, and Dr. N. G. Marshall, director of anæsthesia.

Royal Adelaide Hospital, Australia. M. J. W. SANDO
J. R. LAWRENCE.

1. Lassen, H. C. A., Henriksen, E., Neukirch, F., Kristensen, H. S. *Lancet*, 1956, i, 527.



A NEW PINK DISEASE

SIR,—Since mercury was withdrawn from "teething-powders", pink disease in this region has almost disappeared. But a new syndrome has appeared which has claims to usurp the discarded title.

CASE 1.—A baby boy began to vomit intermittently and stopped gaining weight at 6 months of age. He was referred to hospital in his 30th week, when he looked reasonably well, weighing 17 lb. There were no abnormal physical signs. The mother said his napkins turned bright pink when washed. This was specially noticeable with soiled napkins and less so with urine-soaked ones. The colour appeared as soon as the napkin was placed in soapy water, but napkins belonging to a baby cousin, put into the same water, remained white. The mother denied that the child had had any liquid paraffin emulsion, 'Petrolagar', 'Agarol', or any other medicine at all.

CASE 2.—A baby girl, aged 8 months, had had sudden recurring attacks of crying, sweating, and drawing up of the knees for 3 weeks. The bowels were regular, and there had been no vomiting. There were no abnormal physical signs and the baby's weight was 21 lb. 10 oz. The mother had been in the habit of giving her magnesia two or three times in each week and she was advised to stop this. A week later she said that there was no improvement and the baby was still having two or three attacks every day. On this occasion she also remarked that the baby's soiled napkins turned bright pink when put into

2. Mollaret, P., Bastin, R., Damoiseau, B., Goulon, M., Pocidalo, J. J., Rapin, M. *Pr. méd.* 1955, **63**, 1413.
3. Wilson, P., Martin, F. I. R., Last, P. M. *Lancet*, 1956, ii, 442.
4. Last, P. M., Nicholas, J. *Med. J. Aust.* 1956, ii, 373.
5. Tinsley, J. C., Jr., Moore, C. V., Dubach, R., Minnich, V., Grinstein, M. *J. clin. Invest.* 1949, **28**, 1544.

the washtub. As in the first case, all aperients and medicines, apart from the magnesia, were denied.

The solution to both problems came on subsequent occasions in response to a very specific question, " Do you give the baby teething-powders? ". For both mothers this was apparently so normal and usual an administration as not to count as a " medicine ". They were advised to stop giving teething-powders and the symptoms in the babies ceased.

In early editions of *The Extra Pharmacopœia*, ' Steedman's Soothing Powders ' were said to have an average weight of gr. $2^4/_5$ and to contain 27% calomel. In the most recent edition they are said to weigh gr. $2^1/_2$ and to contain no calomel, but 32·61% of phenolphthalein—that is, more than gr. $^4/_5$. Compared with other purgative preparations containing phenolphthalein this is a substantial dose for an infant of 6 months. Emuls. paraff. liq. et phenolphthal. *B.P.C.* contains less than gr. $^1/_5$ per drachm, a usual dose for a child of this age. 'Petrolagar (Red Label)', a proprietary equivalent, has a similar amount, although 'Agarol', another, contains more. Tab. phenolphthal. co. *B.P.C.*, and 'Alophen Pill', a proprietary equivalent, contain only gr. $^1/_2$, although they also contain aloin gr. $^1/_4$. No-one would suggest that a single dose of phenolphthalein gr. $^4/_5$ is likely to harm a young infant, but presentation as a " soothing-powder " may well encourage regular, even daily, administration by some mothers, and increasing administration if the child is other than soothed.

Unless the administration of " soothing-powders " is specifically asked about, the explanation of the vomiting or colic may remain obscure. This syndrome could be even more perplexing if the napkins were washed with soaps or detergents less alkaline than those used in the two cases presented here.

Department of Child Health,
University of Durham,
at Newcastle upon Tyne.

E. G. KNOX.

EFFECT OF HEAT ON SPASTICITY OF DISSEMINATED SCLEROSIS

SIR,—A phenomenon which, as far as I know, has not been recorded is that spasticity is much increased when patients with disseminated sclerosis are exposed to high temperatures. This condition is easily corrected by reducing the blood temperature below normal by a cold shower or bath.

Disseminated sclerosis may be caused by a thrombocyte-agglutinating substance in the cerebrospinal fluid. Persson [1] suggested that penetration of this agglutinating substance into the small veins of the central nervous system may be responsible for the periventricular thrombus formation and also for thrombosis in the small veins of the central nervous system. Increase in plasma-fibrinogen during the active phases of the disease may also contribute to thrombus formation.

In view of the increase in prothrombin-times following the exposure of man to wet thermal atmospheres,[2] over 30 cases of disseminated sclerosis, varying from mild to severe, were treated under these conditions combined with anticoagulant therapy. The severe cases became so spastic that further treatment was impossible, while in the less severe cases favourable results were obtained.

All these patients said that their weakness and spasticity increased in warm weather and that they felt better in the cold. It was noted that all mouth temperatures were subnormal.

It is interesting to note that disseminated sclerosis is more prevalent in temperate climates than in the tropics, and this raises the question whether this condition is connected with lower metabolism, blood temperature, and thrombus formation.

Tunbridge Wells. E. F. ST. JOHN LYBURN.

1. Persson, I. *Arch. Neurol. Psychiat.* 1956, **76**, 343.
2. Lyburn, E. F. St. J. *Lancet*, 1957, ii, 745.

CORTISONE IN THE TREATMENT OF ACUTE INFECTIONS

SIR,—I am disappointed that none of my colleagues has so far responded to my invitation (Nov. 16) to come forward with his experience of cortisone in the acute infections, the more so as some, I know, have been using it. Meantime, as I have been accused of using it in " hit-or-miss " fashion, and as I have had a number of letters from doctors, may I put forward my views in a little more detail?

Let me concede at once that experiment and experience alike suggest that, should infection be sustained—or introduced—under cover of cortisone, the results may be disastrous inasmuch as the defences may be subdued and signs and symptoms of what is afoot may be minimal until irreparable damage has been done. The position, however, is vastly different once the defences have been seriously challenged and aroused. Here, in a certain number of cases, the situation is reversed, and the danger arises, not from the sluggishness of the body's reaction, but from its unbridled vigour.

In any epidemic, it is reasonable to assume that the infective agent is of uniform virulence and invasiveness. Those infected may be divided into (1) the insusceptible or immune who do not react at all, followed in ascending order of susceptibility by those who experience (2) subclinical, (3) mild, (4) moderate, or (5) severe attacks. Finally (6) there are hyper-reactives who might be described as allergic to the parasite and who may kill themselves—and frequently do—by the vehemence of their response as expressed in hæmorrhages (into the adrenals and elsewhere), collapse, exudates, effusions, adenopathies, intractable vomiting and diarrhœa, and so on, unless something is done to curb the reaction. It is here that cortisone is invaluable, and so frequently saves life. Such fulminating reactions occur most commonly in meningococcal infections (Waterhouse-Friderichsen syndrome) and probably also in certain cases of smallpox and hypertoxic diphtheria, but it appears they may also occur in other conditions—e.g., the cases described by Dr. Barrowcliff and Dr. Prior (Dec. 14) and Dr. Warrack (Dec. 21) where the parasite was presumably the influenza virus.

Obviously, when using cortisone so early in the infective process, two questions are of prime importance. Firstly, does cortisone inhibit the action of the antibiotics and, secondly, does it hinder the development of immunity? As regards the first, I can only say that if it does I have not been able to detect it clinically. In respect of immunity, it is only reasonable to assume that cortisone will retard its development, but I know of no real evidence on the subject. In any event, since the only alternative to its use in these cases is a fatality, the question seems of academic importance.

Neither of these considerations apply when invoking cortisone at a later stage in the infective process when, in spite of days or more commonly weeks of therapy, the patient is going steadily downhill and a fatal outcome seems inevitable. Whether in such cases a gradually developing adrenocortical exhaustion is a major factor in this decline and, if so, why one adrenocortical steroid out of approximately a score should apparently prove competent to arrest it are questions I am unable to answer, but the fact is that cortisone has turned the tide in far too many cases to admit of coincidence as a reasonable explanation. Perhaps, however, instead of theorising, I may quote a few representative cases.

The value of cortisone in the Waterhouse-Friderichsen syndrome is no longer in dispute. There are numerous references to it in the literature and I myself with others have chronicled two cases.[1] I will therefore confine myself to its use in other conditions.

1. Breen, G. E., Emond, R. T. D., Walley, R. V. *Lancet*, 1952. i, 1140.

The first case was an infection with an unidentified pyogenic organism (possibly a resistant staphylococcus). The second was probably an erythema multiforme, and the last two are examples of glandular fever, presumably virus in origin.

CASE 1.—A man of 33, admitted on March 18, 1956. A month previously he had food-poisoning on board ship to New York where he had treatment with some improvement. Diarrhœa recurred on return voyage, complicated by melæna shortly after arriving home. On admission he was sharply febrile and very ill. During subsequent days, severe hæmorrhages from the rectum. Found to have ischiorectal abscess with fistula-in-ano, and ? early peritonitis. Blood-transfusion on March 20 followed by laparotomy which revealed turbid fluid in the peritoneal cavity. Abscess laid open at the same time. No pathogens grown from either source. After operation high fever persisted with copious oozing from abscess cavity and by March 27, despite treatment including frequent transfusions, the patient was moribund. Placed on intravenous glucose drip with cortisone (120 mg. in twenty-four hours) and erythromycin. Response immediate. Within twenty-four hours patient afebrile, mentally clear, sitting up, and taking nourishment by mouth. Following further transfusions, colostomy on April 13, closed on June 22. Discharged fit on July 9.

CASE 2.—A boy of 16, admitted on Nov. 12, 1955, ill since Nov. 3. On admission, sharply febrile, profuse desquamation of face and trunk together with (*a*) Stevens-Johnson syndrome (stomatitis, conjunctivitis, and urethritis); (*b*) meningism; (*c*) paraplegia of lower-motor-neurone type; (*d*) arthritis of right hip; and (*e*) acute enteritis. Lumbar puncture: 12 cells per c.mm., fluid otherwise normal. Urine normal. Condition deteriorated steadily. Nov. 17, pericardial effusion. Nov. 18, effusion in both knee-joints, and cortisone (25 mg. t.d.s.) begun. Immediate response. Afebrile within twelve hours. By Nov. 23 power had returned to legs, and heart-sounds were normal. Discharged fully recovered on Jan. 10.

CASE 3.—A girl aged 19, admitted April 10, 1957, the twelfth day of a severe attack of glandular fever. Fauces and tonsils very œdematous and covered with membrane, gross cervical adenitis (bull neck), and copious bloodstained nasal discharge. Severe anæmia (Hb 40%). As she could not swallow and her nose was impassable to a catheter, she had to be maintained intravenously. Her condition deteriorated steadily despite several transfusions. On April 13 there was much albuminuria with widespread crepitations over both lungs and by April 16 she appeared moribund (racing feeble pulse, peripheral cyanosis, and delirium). Cortisone (125 mg. in twenty-four hours) included in drip, again with an immediate response. Within twenty-four hours the temperature had fallen and in forty-eight hours the throat and glands had much receded and she was taking food by mouth. Subsequent progress uneventful. Discharged well on May 15.

CASE 4.—A similar case of glandular fever. A boy of 8 years, admitted on Oct. 10, 1957. There was high fever, gross angina, bull neck, copious nasal discharge, and the patient was stuporous. Prednisone (10 mg. t.d.s.) was begun at once. On the following day I failed to recognise the patient. His temperature was normal, the glands were scarcely visible, and the nasal discharge had ceased. He was sitting up in bed making a hearty dinner. I have included this case because anyone who has seen a florid and actively developing infectious reaction virtually obliterated in twenty-four hours (without elimination of the organism) can hardly fail to question much of our current theory on the genesis and purpose—if any—of such reactions, and indeed of the whole nature of infectious disease in general.

I have now used cortisone or its derivatives in some 70 selected patients over the past five years. Most were P.U.O.S for which, despite diligent inquiry, no cause could be found; some showed the stigmata of collagen disease. But there were many others: lung and bowel infections (including infantile gastroenteritis) and infections of the central nervous system (*Hæmophilus influenzæ* meningitis, pneumococcal and meningococcal meningitis, and an extreme rarity, a monkey-B2-virus encephalomyelitis). I have used it with restricted objectives: to reduce gross palpebral œdema in herpes ophthalmicus with iritis and corneal ulcer; to control copious secretions in a case of bulbospinal poliomyelitis on intermittent positive-pressure respiration. (Intimidated by experimental reports, this is the only case of poliomyelitis in which I have had the courage to use it so far.) Very seldom have I been disappointed. I was not impressed by the response in a case of (probable) polyarteritis with peripheral neuritis, nor had it any observable effect in a case of hæmorrhagic chickenpox (thrombocytopenic) with severe recurrent epistaxis. Only once have I had reason to suspect a harmful side-effect—in a man of 78 admitted pulseless and semicomatose, with widespread bronchopneumonia who died thirty-six hours after admission. At necropsy there was fairly free bleeding from a recent peptic ulcer which may or may not have been due to prednisone.

The last thing I wish to do is to encourage the indiscriminate use of cortisone or its derivatives. But I submit that we have here a weapon of immense power in the treatment of the acute infections which not only saves life but has much to teach us by what it does and, perhaps still more, by what it fails to do. It is surely essential that its applications and limitations should be clearly defined as soon as may be. At present there is obviously much confusion. Thus a recent "authoritative" review states that cortisone is contraindicated in tuberculosis. This contrasts strangely with the findings of the Research Committee of the Tuberculosis Society of Scotland [2] which showed that prednisolone-treated cases did better than the controls without it. We need more reports of this type based on careful clinical trials rather than on conjecture or misleading animal experiments. Once again, therefore, I would appeal to those who have used cortisone in the infections to give us the results of their experience.

South Middlesex Hospital, Isleworth. G. E. BREEN.

SIR,—The possible use of cortisone in influenzal pneumonia has lately been discussed in your columns, and I should like to record the following unhappy experience.

An Arab, aged about 40, came to hospital because of fever, cough, rusty sputum, and pain in the chest for two days. X-ray examination showed bilateral basal pneumonia. Temperature 102° F. White-cell count 4800 per c.mm. Erythrocyte-sedimentation rate 25 mm. in 1st hour. Generalised rhonchi and coarse râles in the chest.

During a secondary epidemic of influenza, a diagnosis could be made with some certainty. The antibiotics chosen were streptomycin and isoniazid because it was felt that an underlying tuberculous infection could not be ruled out. Penicillin was added after four days because there had been no response to streptomycin; but no clinical benefit followed.

It was then decided to give the patient hydrocortisone (50 mg. intramuscularly three times a day). His condition thereupon rapidly deteriorated: dyspnœa became the most prominent symptom, pulse and temperature soared, and a radiograph showed almost total consolidation of both lungs. The patient died twenty-six hours after the first dose of hydrocortisone.

It is unreasonable to draw conclusions from one experience, but this case supports the view expressed by Dr. Librach (Dec. 7).

Qatar, Persian Gulf. R. T. S. LOUTTIT.

2. *Brit. med. J.* 1957, ii, 1131.

MANIPULATION FOR BACKACHE

SIR,—We should like to congratulate Mr. Bremner on his article of Jan. 4 dealing with manipulation in the management of chronic low backache due to "lumbosacral strain".

We agree that the lesion of lumbosacral strain is a degeneration, most commonly of the L5/S1 disc (we include the L4/L5 disc less commonly), with involvement of the posterior joints by laxity at first, followed by osteoarthritis.

Before any form of treatment is contemplated a more exact diagnosis should be attempted. Claims for the replacement of a slipped disc are often made when the condition is really due to involvement of other structures forming a spinal segment; or when, in the older patient, the condition is the result of an aggravation of a pre-existing spondylosis, signifying itself in disc degeneration and osteoarthritis.

The value of any form of treatment and the prognosis will depend on the type of onset, the phase the condition is in at the time of treatment, the patient's age, the effect of previous treatment, and the type of sciatica (true or pseudo).

Certainly, manipulations without anæsthesia, especially as carried out by Dr. Hargrave-Wilson (Jan. 11), can help in many cases, but it is our contention, in support of Mr. Bremner, that manipulation with anæsthesia also has a place in the treatment of certain cases.

Manipulations without anæsthesia should never be carried out forcibly against severe muscle spasms, but if they are performed gently, especially when previous muscle spasm has been reduced by heat, massage, spraying with ethyl chloride, or procaine injection, they often relieve symptoms immediately. Muscle spasm, denoting joint irritation, must be coaxed rather than forced. No sensible medical practitioner will rely on any one form of treatment in this condition.

It must be remembered that the lumbosacral region is one of the prime fixing levels in the body, because it is at the junction of the trunk and the pelvis. Remedial exercises and postural training are, therefore, an essential part of treatment.

Low back pain may be a symptom in the following groups of patients:

(1) Those with postural and occupational strain, causing first, muscle strain, then joint strain. This condition can begin at any time but usually shows itself before the age of 25. Manipulation under anæsthesia is often indicated in the younger athletic patient, with a history of injury some months previously, who has pain on movement in one direction only.

(2) Those with low back pain, of acute onset, associated with lumbago and sciatica. This denotes a joint strain in which one or more of the components of a vertebral segment have become involved, either by injury or in a degenerative process. The average age for this type is 25–35. In this group it is of paramount importance to distinguish between a true sciatica and a pseudo-sciatica. Patients with lumbago only often get better in three weeks, but manipulation without anæsthesia can often relieve the symptoms in a few days. If there is true sciatica no experienced doctor is likely to recommend manipulation under anæsthesia until he has tried every form of conservative treatment and is prepared to operate immediately, especially if the symptoms are aggravated. In this type of case disastrous results may follow any type of manipulation, for a piece of sequestrated loose disc may be pushed further backwards through the posterior longitudinal ligament, with pressure on the cauda equina or sciatic roots. Untreated patients of this group tend to pass into the next group.

(3) Those with chronic lumbosacral strain (without radiographic evidence of spondylosis) signifying disc degeneration and osteoarthritis. This is the group which Mr. Bremner is considering, the average age being 39 in his male patients and 36 in the females. The first group may gradually pass into this group, or an acute exacerbation may produce group 2. If the condition is due to a lesion of the apophysial or posterior intervertebral joints, immediate relief may be expected from manipulation without anæsthesia. By appreciation of certain physical signs and symptoms, one can diagnose many of these lesions and expect an immediate result. If the patient fails to improve after manipulation without anæsthesia, it is well worth trying the effects of a controlled manipulation under anæsthesia before resorting to disc operation or spinal fusion.

(4) This includes those patients with chronic lumbosacral strain and radiographic evidence of spondylosis. Most are over 50. Manipulation without anæsthesia can play an important part in the relief of symptoms. An acute exacerbation, through an unguarded movement, may give rise to lumbago, true sciatica, or pseudo-sciatica.

Let us always try to be more specific in our diagnosis. Are we dealing with a muscle strain or joint strain with or without disc involvement? Is the disc involvement an internal derangement between the vertebral bodies, or an external prolapse through the posterior longitudinal ligament, or is there an aggravation of a pre-existing spondylosis? Many patients are improved by bed rest, a plaster jacket, various forms of support, manipulation, injections, various types of physiotherapy, elimination of septic foci, or treatment of gout. The psychiatric approach and deep X-ray therapy must not be despised. Operation in the chosen case may become essential and can give a degree of permanent relief of symptoms obtained by no other method.

The conditions of low back pain pass through so many phases; it is only by careful assessment of the signs and symptoms of these that the right treatment can be arrived at.

W. E. TUCKER
R. P. GOULDEN.

London, W.1.

TREATMENT OF HEPATOCEREBRAL INTOXICATION

SIR,—The treatment of hepatocerebral intoxication by influencing the urea cycle and related reactions has been very encouraging in our experience of over one year. Some of the implications of present knowledge of the urea cycle [1] seem not to be fully appreciated. We should like, therefore, to emphasise the following points.

Ammonia is converted into urea only in the liver at the steps involving the transformation of ornithine into citrulline: $CO_2 + NH_3 +$ A.T.P. + (catalytic amounts of carbamyl glutamate) + ornithine → citrulline.

In a similar reaction, if ornithine is replaced by aspartate and the corresponding enzymes, the active carbamyl intermediate is converted into carbamyl aspartate, which is the first intermediate in the biosynthesis of pyrimidines and, therefore, of nucleic acids. The second nitrogen of urea enters as amino nitrogen (aspartate):

Citrulline + aspartate + A.T.P. → arginine → urea + ornithine.

Thus, for every turn of the cycle, 1 mole of free ammonia, 1 mole of amino nitrogen, and 1 mole of carbon dioxide are transformed into urea via the catalytic action of ornithine and of carbamyl or other N-acyl glutamate derivatives (acetyl glutamate has been identified as the physiological agent).

The prevention, by arginine, of the toxic effects produced by ammonia administration and those of amino-nitrogen administration cannot be directly compared, since ammonia is converted into aminoacids only by reductive amination of *a*-ketoglutarate followed by transamination.

In normal people the Krebs urea cycle should function with adequate enzymes, intermediates, and substrate concentrations; therefore increasing only one substrate (presumably ornithine from the administered arginine) may not necessarily increase the overall rate of urea formation in the normal liver.

1. Grisolia, S., Ratner, R. B. *in* Amino-acid Symposium. Baltimore, 1955.

Therefore, ideal therapy based on present knowledge should include (*a*) elimination of the source of ammonia, and (*b*) the administration of arginine and carbamyl glutamate, the latter for acute or chronic hepatic failure as well as for liver regeneration.

Since carbamyl glutamate is easier and cheaper to make than acetyl glutamate we have been using this catalytic agent for some nine months (intravenously as 3 g. of the potassium salt combined with 10 g. of arginine, oral dose 1-2 g. daily), with good results. Finally, this treatment may be reinforced by binding the excess ammonia via formation of glutamine analogues in vivo as a temporary measure to aid the overloaded urea cycle. Attempts are in progress to combine these therapeutic measures.

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P.A.S. AND THE PATIENT

SIR,—We should like to comment on the article by Dr. Dixon and his colleagues,[1] in which they report that 50% of their outpatients on P.A.S. therapy have been found, as a result of a single urine test, to have defaulted in taking their P.A.S.

It is generally accepted that P.A.S. prevents resistance to streptomycin and isoniazid, and that its toxicity is low. Its importance in combined long-term treatment has, therefore, never been contested so far. Being administered by mouth, it is particularly suitable for ambulant therapy and for children. Combined isoniazid–P.A.S. has gained further support since it was realised that P.A.S. delays the inactivation of isoniazid by inhibiting its acetylation.[2]

To deal with gastrointestinal disturbances during oral treatment with P.A.S. and isoniazid, two definite improvements have been made: first, by introducing combined preparations in an attempt to overcome the unreliable P.A.S. ingestion [3]; and secondly by evolving P.A.S. preparations based on benzoyl-P.A.S., like calcium B-P.A.S. Owing to their greater acceptability [4] and more satisfactory gastrointestinal tolerance,[5,6] these preparations make uninterrupted P.A.S. therapy easier.

It is surprising, therefore, that Dixon et al. report little or no difference in the "default-rate", whether the drugs are given separately or in combined form, and whether P.A.S. or B-P.A.S. is prescribed.

Your annotation [3] advises examination of the causes of the failure to take P.A.S., before the well-proven ambulant chemotherapy with isoniazid and P.A.S. is dropped. We wonder whether the results obtained under the chosen experimental conditions justify such a far-reaching conclusion. It is hard to tell, because neither the single doses of the P.A.S. preparations nor the time intervals between these doses and the urine analyses are given.

Dixon et al. recommend the ferric-chloride test for the control of both P.A.S. therapy and B-P.A.S. However, on theoretical considerations alone, the colour reaction due to B-P.A.S. is 50% weaker than that due to the same weight of P.A.S., because the benzoyl radical constitutes an important fraction of the B-P.A.S. molecule. On checking Dixon's modified ferric-chloride test in a small number of volunteers, we found that, after administration of 3·5 g. of calcium B-P.A.S., the colour reaction in the urine excreted in the sixth hour after medication was not always positive. After giving 3·0 g. of sodium P.A.S., however, the test was positive and stronger in all cases. It may therefore be possible that Dixon's test is not sufficiently sensitive for B-P.A.S., thus leading to wrong conclusions regarding default of patients taking B-P.A.S. The same applies to the tests involving hypochlorite and Ehrlich's reagent, which were used by Leggat [7] for controlling P.A.S. medication.

To make it suitable also for controlling B-P.A.S. treatment, the test cannot be rendered more sensitive under Dixon's experimental conditions by diminishing the dilution of the urine, for basic iron salts precipitate and interfere with the reaction.

The sensitivity may, however, be increased by adjusting the pH to 2·5–3, which is optimal for the reaction and within which range less iron phosphate is precipitated. With the aid of a glycine–HCl buffer of pH 2·5, urine can be diluted 1 : 30, in which dilution neither alkalinity nor excessive urinary phosphates will interfere with the ferric-chloride reaction. Since, however, B-P.A.S. is sparingly soluble at this pH, the buffer must contain ethyl alcohol. The following buffer is suitable for use in testing for both P.A.S. and B-P.A.S.

Glycine (aminoacetic acid)	1·728 g.
Sodium chloride	1·350 g.
0·1 *N* Hydrochloric acid	270 ml.
Distilled water	230 ml.
96% ethyl alcohol	500 ml.

Should the pH of the buffer differ from 2·5 by more than 0·5 units, it must be corrected by adding a few ml. of either 0·1 *N* hydrochloric acid or sodium hydroxide.

To check whether P.A.S. or B-P.A.S. is being taken, 0·1 ml. of urine is diluted with 3 ml. of glycine buffer, and 1 drop of ferric-chloride solution (3 g. of $FeCl_3 \cdot 6 H_2O$ in 100 ml. of distilled water) is added. In the presence of P.A.S. derivatives, a red-violet colour results. If, in urine containing large amounts of phosphates (e.g. morning urine), clouding is observed due to precipitation of iron phosphate, the reaction is produced by adding one more drop of ferric-chloride solution.

Unlike Dixon et al. we have found that their ferric-chloride test on subjects who had been given 1 g. of aspirin was positive in the urine excreted in the sixth and in the twelfth hour after medication.

The intention of these comments is, first, to suggest that, in certain circumstances, Dixon's modified ferric chloride test may be fallacious as regards the detection of B-P.A.S. defaulters and to suggest an improvement of his method; and, secondly, we should be happy if this would help to re-establish, at least in part, the honour of the patients who were suspected of making misleading statements.

H. LAUENER
T. FRIEDRICH.

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SYLLABUS FOR EXAMINATIONS IN PSYCHOLOGY

SIR,—I am a senior clinical psychologist in a mental hospital who, as part of her duties, tries to give some help to doctors who are preparing to take their D.P.M., part I, in which psychology is one of the subjects.

Psychology is not an easy subject for people trained in medicine, because it uses different concepts and a different vocabulary. Furthermore, its boundaries are extremely wide, and the English Conjoint Board does not publish a syllabus to guide candidates in their studies. If they turn to previous papers for guidance they find little help, since within the past two years questions have been set on as widely varying topics as the electroencephalograph, the value of the concept of psychosomatic disorder in general practice, and the theory of the structure of consciousness by Janet. Two of these topics come only very generally within the confines of psychology, and the third is of academic interest only, as the relevant work was published in 1890. One would not quarrel with this so much if there were a published syllabus to some item of which the question could legitimately refer.

1. Dixon, W. M., Stradling, P., Wootton, I. D. P. *Lancet*, 1957, ii, 871.
2. Favez, G., Lauener, H. *Schweiz. med. Wschr.* 1956, **86**, 1395.
3. *Lancet*, 1957, ii, 881.
4. Gibson, M. O. J., Nagley, M. M. *Tubercle*, 1955, **36**, 209.
5. Hudson, E. H. *in* Heaf, F. R. G., Symposium of Tuberculosis; p. 321. London, 1957.
6. Stahle, I. *Acta. tuberc. scand.* 1957, **34**, 83.
7. Leggat, P. O. *Lancet*, 1957, ii, 1283.

This problem is particularly acute for doctors who are working on their own in provincial hospitals, and whose contacts with universities and access to big libraries are limited to occasional visits to London.

As the universities publish syllabuses for their D.P.M. psychology examinations, cannot the Conjoint Board do the same?

St. James' Hospital, Portsmouth. A. M. SILVER

NYLON-DARN REPAIRS OF HERNIÆ

SIR,—I should like to mention a stern test I gave the nylon darn in 1952.[1]

This concerned a man of 82 who came to Nottingham General Hospital with an inflammatory mass in the right upper scrotum, which was found to be due to an appendix abscess in a hernial sac. Having removed the appendix and excised the sac I carried out a single layer darn, using no. 8 monofilamentous nylon. No. 5 nylon was used to close the external oblique. The wound healed with only a mild superficial infection, and when I last heard from the patient a year later there had been neither recurrence nor sinus trouble.

Satisfactory healing under such unfavourable conditions bears out Mr. Moloney's original contention that "nylon tends not to be disturbed by the misfortune of sepsis".

Dublin. VICTOR LANE.

Parliament

The Minister's Review

ON March 5, moving the second reading of the National Health Service Contributions Bill, which was carried by 308 votes to 252, Mr. DEREK WALKER-SMITH, the Minister of Health, took the opportunity to discuss some of the general issues of the economics of the service. The cost of the service has risen from £452 million in 1949–50 to £740 million, and he began by pointing out that this increase of £288 million, allowing for changes in the value of money, was an increase in real terms of £80 million.

Another way of measuring the cost of the service was as a percentage of the gross national product, and this percentage, which had been dropping for some years until 1954, had since risen slightly. He himself distrusted this percentage as a ready reckoner of the health and progress of the service. He believed that we should aim to expand the gross national product as much as possible and spend on the health service the highest common factor of what we needed and what we could afford. The ideal situation would be to get a sustained and rapid increase of the national product coupled with a sustained and steady fall in calls on the health service owing to the reduction of illness, yet that ideal situation would lead to a declining percentage. Conversely if the gross national product fell the percentage spent on the service, though the money was actually static, would rise. Yet this would not mean that the health service was doing better but merely that the country was doing worse.

Returning to the present increase of £288 million, he pointed out that since in terms of real money this was only an increase of £80 million, we were left, after making minor adjustments to allow for the increase in the population and in the proportion of old people, with £200 million which was due to inflation. It was not the prodigal habits of the service which were forcing the inflationary pace. The increase reflected the inflationary tendencies in the economy as a whole.

Measured in terms of services rendered as well as in terms of money spent, the contributor, in Mr. Walker-Smith's view, was getting good value. Despite our economic difficulties the money available for capital works on hospitals was increasing. Bed occupancy had risen from 453,000 in 1950 to 478,000 in 1956, and outpatient attendances from 31 million to over 35 million. In 1951 there were 20,500 general practitioners, in 1956 22,500; and the number of patients per doctor had fallen from 2500 to 2272. The number of dental treatments had risen from $9^1/_2$ million in 1953 to 12 million in 1956, and of sight tests from $4^1/_2$ million in 1951 to $5^1/_2$ million in 1956.

The increased productivity and value of the service was not of course inconsistent with the possibility of economies being found without detriment to the patient. Could the inflationary increase, or any substantial part of it, be met by economies in the service, apart from the general arrest of the inflation in the economy as a whole? The pattern of expenditure according to the 1958–59 estimates was: hospital running costs £399 million (about 54% of the total cost); hospital capital cost £23 million (3%); general medical services £72 million (10%); pharmaceutical services £74 million (10%); dental services £51 million (7%); local authority services £65 million (9%). Thus more than half the money went on hospital running costs; these were mainly wages and commodities and the rise in their cost reflected the general inflationary tendency. There remained the possibility of economies in administration, and to that end he had instituted the technique of "organisation and methods" in hospitals in the hospital service. It was started in September, 1954, with an experimental hospital organisation and methods unit recruited from the Treasury and the Ministry. By September last this unit had completed 78 assignments covering a large number of aspects of hospital work at individual hospitals. It had also undertaken, and had nearly completed, 8 comparative studies involving the examination of important common procedures or services at a large number of hospitals. The subjects included under these comparative studies were methods of analysing expenditure, arrangements for compiling and maintaining inventories, methods of stores accounting and arrangements for outpatient departments. The experience of these three years had shown that the application of the various techniques used by organisation and methods investigation in business, industry, and public administration could produce valuable results in the hospital field. The value of this work had been recognised by the Estimates Committee, and he was now considering the best way to establish organisation and methods procedure as a permanent and integral part of the hospital service.

He realised that there was some doubt or even disquiet about the size of the drug bill which, at £74 million, had more than doubled since the start of the service. There were two causes: the general rise in costs, and the introduction of new drugs. But the new drugs had made a great contribution, not only in the social sense, but also to the national economy in mitigating the effects of diseases like tuberculosis, pneumonia, and acute rheumatism. They were keeping the drug bill under scrutiny and trying to confine it to its lowest reasonable cost.

It was clear, he thought, that the main element in the steady, and hitherto apparently uncontrollable, rise in the cost of the health service was a reflection of the general inflationary tendency in the economy. The health service clearly had a prime interest in countering and reversing inflation, because only so could it hope to achieve its own economic stability and salvation, and the principle of unlimited Exchequer liability was clearly inconsistent with a disinflationary policy. It was in the context of these principles that the modest adjustment in the pattern of payment contained in this Bill must derive its justification. In no other country was the scale of service equal to ours. In most countries it was done mainly on the basis of health insurance rather than on the basis of a national scheme, and in few countries did even health insurance cover all. Often, even in enlightened and progressive countries like the Netherlands, France, and Western Germany, the Government contributed nothing to the insurance scheme.

For ten years the efforts to control expenditure on the health service had been rather makeshift and piecemeal. We had been working our way rather as in a tunnel, with our eyes fixed not much further forward than our feet. He believed

1. Lane, V. *J. Irish med. Assoc.*, 1954, **35**, 284.

that we could now see some light at the end of the tunnel and a sounder financial future for the service. To many it was a paradox that its improved efficiency, productivity, and output was not reflected in a diminution of disease and consequent diminution of treatment and cost. The answer was twofold. First, many of the new drugs and treatments were necessarily expensive and the immediate impact was to increase costs. Secondly, because of the war and the consequent arrears the first impact of increased productivity had been to reduce waiting-lists and accelerate treatment. But something of what could be done in the future had been shown by the dramatic reduction in the calls on the hospital service—for example, in the case of tuberculosis. He hoped that this pattern would be repeated in other ways, especially by arranging for community care instead of hospital care for more old people and more of the mentally ill.

The National Health Service could have a sound financial basis only if we got rid of its inflationary elements, and since these reflected the general position, we could succeed only by ridding the whole economy of its inflationary virus. It was not the financial basis of the health service only which depended on this for success. Inflation and the social services could not coexist in the long run. The social services were strong in themselves, but they could not be stronger than sterling.

Medicine and Television

On March 7 Mr. ERNEST MARPLES, the Postmaster-General, made the following statement :

At question time on Feb. 26 [1] I referred to the B.B.C.'s consultation with medical authorities about the programme *Your Life in Their Hands*. This seems to have given rise to some misunderstanding I would like to clear up this misunderstanding.

I am informed by the B.B.C. that the Corporation had had wide and detailed discussions with medical, surgical, and nursing staffs both on the subject matter of the programmes as well as their method of presentation. Before the first broadcast, the B.B.C. held a conference. At this conference, representatives of the Royal College of Surgeons and the Royal College of Physicians and members of the College of General Practitioners were present, together with other interested medical men and representatives of the medical Press. Nothing occurred as a result of this informal consultation to suggest to the B.B.C. that its programmes would meet with opposition from the bodies concerned or that the Corporation ought not to proceed with its plans. Correspondence after the first broadcast from members of the medical profession and others confirmed the B.B.C. in this view.

I regret that the information I previously passed on to the House implied a more formal degree of consultation between the B.B.C. and the medical bodies mentioned as well as a formal expression of their subsequent appreciation of the programme. This appears to have arisen from a misunderstanding between my department and the Corporation.

QUESTION TIME

Senior Registrars

Mr. KENNETH ROBINSON asked the Minister of Health when he expected to meet the Joint Consultants Committee to discuss the senior registrar problem.—Mr. DEREK WALKER-SMITH replied: Tuesday, March 25.

Mr. ROBINSON: Will the Minister, since there has been an effort over a long period to reach an agreed solution in this matter, give an assurance that he will, if necessary, impose his own just solution on the profession and see that no medical or vested interests are allowed to stand in the way of its implementation?—Mr. WALKER-SMITH: I would not like to enter into a discussion of this sort on any assumption other than that reason will prevail and that we shall get an appropriate and reasonable solution harmoniously by agreement together.

Mr. JOHN CRONIN asked the Minister on how many occasions representatives of his Department have had meetings with the Joint Consultants Committee during the last two years to discuss the difficulties of senior registrars in the National Health Service.—Mr. WALKER-SMITH replied: There have been ten meetings at which the general question of hospital medical staffing, including the senior registrar aspect, has been discussed.

Mr. CRONIN asked the Minister why he had made it a condition for relieving the difficulties of senior registrars that the medical profession should agree to the setting up of a number of new special posts, not previously provided for in the National Health Service, in which the duties were similar to those of consultants, whereas the salary and status were substantially inferior to those of consultants.—Mr. WALKER-SMITH: No such condition has been made.

Cost of Prescriptions

Mr. ARTHUR BLENKINSOP asked the Minister of Health what was the average cost per prescription issued under the National Health Service as at the latest available date; how this compared with the cost one year and two years previously; and what analysis had been made to establish the cause of any increase.—Mr. WALKER-SMITH replied: Approximately 6*s*. 1*d*. in December, 1957, as compared with 5*s*. 6½*d*. in December, 1956, and 4*s*. 7½*d*. in December, 1955. Examination of representative samples of prescriptions shows that the main reason for the increase in December, 1956, and subsequently was the prescribing of larger quantities. Since December, 1955, the cost has also been affected by the prescribing of certain expensive preparations which had not previously been available. Mr. BLENKINSOP: Does the Minister not recognise that this is a confession that the increased prescription charge has resulted in higher costs to the nation because of the larger quantities his Department encourages doctors to prescribe? Will he not meet the problem sensibly by withdrawing the charge?—Mr. WALKER-SMITH: Although there is a higher prescription charge, partly due to the larger quantities but also partly due to the new drugs, the number of prescriptions in 1957, even with the influenza epidemic, dropped substantially below the number of prescriptions in the previous year. Mr. BLENKINSOP: Does not the Minister agree, in spite of the fact that there is a reduction in the number of prescriptions, that the increased quantities in prescriptions have resulted in a very considerable increased charge to the community, and therefore does he not agree it is time we abolished the charge?—Mr. WALKER-SMITH: I do not think that conclusion follows from the position as we have it now. There are certain respects in which the prescription of large quantities is justifiable. If there is over-prescription on unjustifiable occasions, that is one of the things we shall hope to deal with after having the advantage of the advice of Sir Henry Hinchliffe's Committee and any other advice we may receive.

Number of Dentists

It is estimated that by July 5, 1958, about 1500 dentists in general practice, who will have reached age 60 or more, will then be entitled to retire on pension under the National Health Service Superannuation Regulations on completing ten years' service.

Private Practices

Mr. BLENKINSOP asked the Minister of Health on what basis it was assumed that earnings from private practice by general practitioners amount to £2 million a year and that this figure has remained unchanged since 1948.—Mr. WALKER-SMITH replied: The figure of £2 million has been used in the calculation of the central pool because Mr. Justice Danckwerts adopted it in his award. From and including the financial year 1952–53 it has been used on a provisional basis and is subject to retrospective adjustment should it be found by inquiry to have been too high or too low.

Organisation and Methods Service

Sir KEITH JOSEPH asked the Minister how many staff were engaged in the Hospital Organisation and Methods Service; what assignments were at present being undertaken by it; and whether he could yet announce how much he proposed to extend this service.—Mr. WALKER-SMITH replied: 9. 8 comparative studies and 12 individual assignments are in

1. See *Lancet*, March 1, 1958, p. 539.

hand. In addition, 20 assignments at individual hospitals have been accepted but not yet started. I am considering how, and in what form, this service can best be extended. Sir KEITH JOSEPH: Without exaggerating the virtues of this technique, does not the Minister feel that a staff of 9 is grossly inadequate when put to use in such a vast organisation employing almost the third largest manpower force of the whole country; and when he comes to consider what he proposes to do, will he bear in mind that much benefit could be gained by circulating the results of each inquiry, as it is held, to comparable institutions so that all may benefit?—Mr. WALKER-SMITH: The last part of the question is really more applicable to the comparative studies than to the individual assignments, because of the variety of circumstances to which the individual assignments relate. The studies so far put in hand result from the experimental unit which was set up to see whether this Organisation and Methods system would be of value in the hospital service. I think it has been clearly shown to be of value, and I am actively considering the best way to make this a permanent feature integrated in the hospital service.

Nurses' Overtime

Mr. FENNER BROCKWAY asked the Minister if he would authorise payments to nurses for overtime duties.—Mr. WALKER-SMITH replied: This question has so far arisen only in respect of mental and mental-deficiency nurses who are already paid for excess hours worked.—Mr. BROCKWAY: While recognising that and that the conditions for nurses have considerably improved, since they are still much lower than those for industrial workers, may I ask the Minister at least to see that their devotion is not exploited by the refusal of payment when they do overtime?—Mr. WALKER-SMITH: No claim for payment of this sort has so far been made for the general nurses, and as far as I know none is contemplated.

Obituary

WILLIAM QUARRY WOOD

M.D., Ch.M. Edin., F.R.C.S.E., Hon. F.R.F.P.S.

Mr. Quarry Wood, who died on Feb. 28, was one of Edinburgh's best-known surgeons and an outstanding exponent of his art. In recent years he had become an elder statesman to whom many of his colleagues turned for sound advice and friendly help.

Born in 1888 at St. Boswells, he graduated M.B. from Edinburgh University in 1911. After serving as a house-surgeon in the Royal Infirmary he took the F.R.C.S.E. in 1914, and later he proceeded to the degrees of M.D. and CH.M., on both occasions winning a gold medal. He was a clinical tutor to the Royal Infirmary before he was appointed an assistant surgeon in 1923. He held this post till 1939, when he became surgeon-in-ordinary. Besides his surgical appointments he was lecturer in anatomy to the University in the old department of anatomy in Bristo Place. For a time he was also assistant surgeon to Chalmers Hospital, and for many years he was consulting surgeon to several of the Border hospitals, notably Hawick and Galashiels. He was surgeon to the East of Scotland Civil Service Nursing Home from its inception till his death.

He was elected president of the Royal College of Surgeons of Edinburgh in 1949. During his two years of presidency many reforms in the domestic affairs of the college were carried through, and in public appearances he upheld the dignity of the office with great acceptance. He was elected to honorary fellowship of the Royal Faculty of Physicians and Surgeons of Glasgow. In 1955 he became president of the Medico-Chirurgical Society and he retired from this post last year.

He leaves a widow and a daughter.

Most students first met Mr. Quarry Wood as their teacher of anatomy, and the regard and affection which so many acquired for him at that stage in their careers was added to when they again met him as a teacher of clinical surgery in their later years. He lectured always without a note, and was obviously a master of his subject. He had an orderly mind, and his presentation of any topic made it seem obvious and inevitable.

His surgical work, for which many must be grateful, was notable for the skill and ease with which it was done. In thirty years I never saw him display any sign of ill temper or irritation, however trying or difficult the operation might be. Under the most demanding conditions his manners remained those of a gentleman and never denoted his inner feelings. In his contacts with his staff he always showed a punctilious regard for good manners and a certain formality of behaviour which never allowed the use of anything but official titles and practically never of Christian names. And at the same time he stimulated both high regard and deep affection, for on rare occasions the kindliness, the simplicity, and the high principles by which he set so much store shone through the veneer of formality that he ever wore, and then his true greatness became evident.

He was a skilful angler. To watch this rather slightly built man wading deep in the Tweed and wielding a sixteen-foot rod with ease and precision was to see the true artist at work.

Edinburgh surgery is the poorer for the loss of a man of such high principles, and yet he probably never realised how much affection and regard he generated not only in his own immediate colleagues but in medical men all over the world who had only known him as students. His conscientiousness and his high sense of duty were obvious to all, but his simplicity and his modesty were only known to his more intimate colleagues, and were the foundations of his greatness.

W.A.D.A.

JOSEPH GEORGE EMANUEL

M.D., B.Sc. Lond., M.B. Birm., F.R.C.P.

ON March 3, in his 87th year, Dr. J. G. Emanuel died in Birmingham, the place of his birth and the scene of most of his active life.

He was the eldest son of the Rev. G. J. Emanuel, a remarkable minister of the Hebrew congregation, and went to King Edward's School and later to the Queen's and Mason Colleges for his training in medicine. In 1891 he took the B.Sc. Lond. and he qualified in 1896, four years before the University of Birmingham was established. After a period of residence in the City of London Hospital for Diseases of the Chest he obtained the M.B. Lond. with honours, and the M.D. in 1901; in the following year he became M.B. Birm. and M.R.C.P. He was elected F.R.C.P. in 1921. An original member of the Association of Physicians, which was founded in 1907, he served on the committee from 1931 to 1933 and was president in 1939.

In 1900 he had returned to Birmingham as pathologist to the General Hospital, where his duties included the post-mortem work, histology, and bacteriology. In 1903 he was elected physician to the Queen's Hospital, and he served it with distinction and wholehearted devotion until he retired at the age-limit in 1931.

In 1930 the death of Laurence Ball left vacant a chair of medicine in the University of Birmingham, and with some difficulty Emanuel was persuaded to undertake the responsibility for four years; his innate modesty made him doubt his fitness for the work and he was surprised and pleased to find that he had the unanimous support of his colleagues and that the students liked him. After retirement from the chair he gave much time to the exacting work of planning and building the new Medical School at Edgbaston and the Queen Elizabeth Hospital. Until recently he was a valuable member of the house-committee of the hospital.

A. P. T. adds the following tribute to his first medical chief:

Emanuel belonged to the generation which witnessed the dawn of the modern revolution in medicine and he told me more than once that he considered he had been exceptionally lucky in the date of his birth. Never, he felt, would there be a period so interesting for a physician as that through which he had passed. Trained at a time when clinical medicine was based largely on an empirical philosophy which regarded experience as the only source of knowledge and when the lack of scientific methods of investigation and of adequate statistical control of therapeutic trials exposed physicians to the temptations of oracular opinions with insufficient rational evidence to support them, Emanuel in his 30s accepted the challenge of the new situation. He carried out for instance some of the first Widal reactions to be done in the Midlands and introduced the sphygmomanometer to his wards and later the electrocardiograph. That eager delight in every fresh advance stayed with him to the end and made him a delightful companion long after he had retired from practice, for he never lost his critical sense, and his comments on what seemed to him spurious were flavoured with a quiet and at times slightly cynical wit. His courage in adversity was remarkable. After an amputation of a foot two years ago he painfully taught himself to walk again and never referred to his disability. To his kindness there was no end, but of that as of his courage no mention was permitted. During the troubled period of Hitlerian persecution of the People of his faith Emanuel was always at the service of his unhappy, displaced brethren and many of them owe to him the reconstruction of shattered lives. To us in Birmingham he has left the inspiration of a fine and devoted life. Stevenson's judgment of a physician as the flower of our civilisation may to some seem over-generous; men like Emanuel, however, suggest that it is sometimes true.

ROBERT KING HOWAT

M.B. Glasg., F.R.C.S., F.R.F.P.S.

Dr. Howat, honorary consulting surgeon to the North Riding Infirmary, Middlesbrough, died at his home in Highgate, London, N.6, on Feb. 9 at the age of 87.

He studied medicine at the University of Glasgow and at the London Hospital. After qualifying in 1892 he held a demonstratorship in anatomy at the School of Medicine in Edinburgh and later house-appointments at the Dorset County Hospital and the Wolverhampton and Staffordshire General Hospital. Soon after he took the F.R.C.S. in 1896, he returned to Glasgow where he became extra dispensary surgeon at Glasgow Royal Infirmary and interim lecturer in anatomy at Anderson College. In 1899 he was elected F.R.F.P.S. Two years later he moved to Middlesbrough, and soon afterwards he was appointed to the honorary staff of the North Riding Infirmary where in due course he had charge of the X-ray, eye, and ear and throat departments. He was also surgeon to the Chaloner Hospital at Guisborough. He was called to the bar in 1914.

In 1932 he retired and moved to London. For a time he was an honorary demonstrator of anatomy at King's College. But ill health forced him to restrict his activities. He had published papers on such varied subjects as minor injuries of the foot, postpartum hæmorrhage, and the health of the private-school child; and in his retirement, though often confined to bed, he began work on his book *Osteology for Dissectors*, which was published in 1950. He leaves a widow.

Dr. J. G. GREENFIELD

Although I met Dr. Greenfield first in 1933 and have been in contact with him on many occasions, it was only during the last five years that I came to know him more closely through joint work, and learned to admire his enormous capacity for work, his profound knowledge of neuropathology in all its historical and cosmopolitan ramifications, his modesty, and his friendly sense of humour. Although he was firmly rooted in the classical past of his specialty, it was impressive to watch him recognise that a new era had commenced with the development of histochemical and ultramicroscopic methods.

In a recent memoir on Thomas Mann his daughter called her father's last year a " year of grace and harvesting despite resolute hard work . . . " One is tempted to apply similar words to the closing period of Dr. Greenfield's life. He certainly did enjoy hard work more than ever, and his harvest has been considerable. It is tragic that he did not live to see his *opus magnum* published.

A. M.

A memorial service will be held at noon on Thursday, March 20, at St. Martin-in-the-Fields.

Diary of the Week

MARCH 16 TO 22

Sunday, 16th

COLLEGE OF GENERAL PRACTITIONERS
11 A.M. *Midland Faculty.* (Powick Hospital, Worcester.) Dr. Denis Williams: What Keeps Us Conscious.

Monday, 17th

UNIVERSITY COLLEGE, Gower Street, W.C.1
5 P.M. Dr. J. D. Judah: Oxidative Phosphorylation; Interpretations and Mechanisms. (Second of two lectures.)
POSTGRADUATE MEDICAL SCHOOL, Ducane Road, W.12
9.30 A.M. Prof. A. K. Basu (Calcutta): Clinico-Pathological Study of Cases of Pulmonary Tuberculosis Treated by Antibiotics and Pulmonary Resection.
4 P.M. Dr. K. G. Lowe: Acute Renal Failure.
HUNTERIAN SOCIETY
8.30 P.M. (Talbot Restaurant, London Wall, E.C.2.) Dr. J. A. Dudgeon, Dr. W. H. Kelleher: Poliomyelitis.

Tuesday, 18th

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
8 P.M. *Pathology.* Dr. Israel Chanarin, Dr. D. L. Mollin, Miss B. B. Anderson: Folic Acid Deficiency. Dr. J. L. Stafford: Hypoplastic Anæmia in Infancy. Dr. Sidney Shaw, Dr. R. A. M. Oliver: Primary Hæmorrhagic Thrombocythæmia.
INSTITUTE OF NEUROLOGY, The National Hospital, Queen Square, W.C.1
5.30 P.M. Prof. N. F. Maclagan: Biochemistry of Coma.
INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, W.C.1
5.30 P.M. Dr. Imrich Friedmann: Microscopical Anatomy of the Ear.
WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY, 91, Dean Street, W.1
5.30 P.M. Mr. K. I. Nissen: Orthopædic Aid for Spastic States.

Wednesday, 19th

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2
4 P.M. *Faculty of Anæsthetists.* Prof. W. D. M. Paton: Mechanisms of Transmission in the Central Nervous System. (Joseph Clover lecture.)
ROYAL SOCIETY OF MEDICINE
5 P.M. *Comparative Medicine.* Dr. D. D. Lawson, Dr. R. N. Smith, Mr. Arthur Naylor: Comparison of Disorders of the Intervertebral Disc in Man and Animals.
8.15 P.M. *General Practice.* Dr. Harold Stewart, Dr. A. A. Mason, Dr. C. A. H. Watts: An Appraisal of Hypnotism in General Practice.
POSTGRADUATE MEDICAL SCHOOL
2 P.M. Dr. R. Winston Evans: Certain Aspects of the Pathology of Ovarian Tumours.
HARVEIAN SOCIETY OF LONDON, 11, Chandos Street, W.1
8.15 P.M. Prof. Robert Kark (Chicago): Bright's Disease Then and Now.
NOTTINGHAM MEDICO-CHIRURGICAL SOCIETY, 64, St. James's Street, Nottingham.
8.30 P.M. Dr. George Day: Fascination of Tuberculosis.

Thursday, 20th

ROYAL SOCIETY OF MEDICINE
4.45 P.M. *Dermatology.* Dr. J. Martin Beare, Dr. G. B. West, Mr. K. W. Head: Mast Cell Disorders.
BRITISH INSTITUTE OF RADIOLOGY, 32, Welbeck Street, W.1
8 P.M. Dr. L. F. Lamerton: Examination of the Clinical and Experimental Data Relating to Possible Hazard to the Individual of Small Doses of Radiation. (Presidential address.)
WEST LONDON MEDICO-CHIRURGICAL SOCIETY
8 P.M. (Star and Garter Hotel, Putney Bridge, S.W.15.) Mr. A. Dickson Wright: Famous Operations in History.
HYPNOTHERAPY GROUP
8 P.M. (1, Wimpole Street, W.1.) Dr. Thomas Main, Dr. Denys Kelsey: Agoraphobia.
UNIVERSITY OF BRISTOL, Royal Fort, Bristol, 8
8.30 P.M. Mr. T. E. Cawthorne: Facial Palsy. (Patrick Watson Williams lecture.)
MANCHESTER MEDICAL SOCIETY
8 P.M. *Anæsthetics.* (Staff House, University of Manchester.) Dr. J. Alfred Lee: Experiences with Extradural Analgesia.

Friday, 21st

ROYAL SOCIETY OF MEDICINE
5 P.M. *Epidemiology and Preventive Medicine.* Air Commodore C. A. Rumball, Dr. H. E. Parry, Dr. J. D. Abbott, Dr. K. B. Rogers: Management of Carriers of Bacteria Causing Intestinal Diseases.
8.15 P.M. *Radiology.* Mr. Harvey Jackson, Mr. J. Jackson Richmond: Pituitary Tumours.
INSTITUTE OF LARYNGOLOGY AND OTOLOGY
3.30 P.M. Mr. G. H. Howells: Cancer of the Larynx.

Notes and News

JAMES SPENCE MEMORIAL

IN response to the appeal for a memorial to the late Sir James Spence, £4840 was subscribed.

From this a gold medal will be awarded by the British Pædiatric Association (every three or four years or less frequently) for outstanding contributions to the advancement or clarification of pædiatric knowledge. For the publication of Spence's collected writings a sum of money has been given to the council of King's College, University of Durham. Contributions from Australia will be used to cover the cost of modelling and casting in bronze a portrait head of Sir James, to be placed in the children's department of the Royal Victoria Infirmary, Newcastle upon Tyne, and ultimately in the new Children's Hospital when that is built. A replica of the sculpture has been presented to the Australian Pædiatric Association, whose foundation was in part stimulated by his visit in 1948. The residue of the fund will be handed to the council of King's College for the creation of a prize in pædiatrics open annually to students, for "an essay of not more than 3000 words on any subject related to pædiatrics which has excited his or her interest and observation during undergraduate studies."

THE FIRST McMURRAY LECTURE

THE late T. P. McMurray was professor of orthopædic surgery in the University of Liverpool from 1939 to 1947, and a lectureship in his honour was established in 1955. It is fitting that the first lecture [1] should have been given by Prof. Bryan McFarland, his successor, and that it should deal with his life, work, and personality.

McMurray was trained by Robert Jones, and succeeded him as director of orthopædic studies in the University of Liverpool in 1933; in 1939 he was appointed as the first professor. Though he played a great part in building up specialist orthopædic services, he strongly advocated their retention in general hospitals, and pressed for undergraduate instruction in the subject.

He was impatient of frills, Professor McFarland tells us, and would say "You mustn't do it" rather than "under all the circumstances it might be inadvisable to proceed in such a way"—which earned him a reputation for gruffness. His surgery, too, was direct and purposeful. He was cautious, or "canny", with such innovations as the use of metals in bone; and he stuck to his beliefs. "To his friends he sometimes seemed intransigent, to his critics stubborn, and to his enemies impossible. He was of an age of independent authority and independent responsibility." His operation of osteotomy for osteoarthritis of the hip has proved effective, though the reason why it relieves pain is not obvious, and it is receiving renewed attention now that some arthroplasty operations have proved disappointing. He wrote books, but his influence was exerted mainly by direct precept; "for those who came under his spell its effects will last for ever."

GUY'S HOSPITAL DENTAL SCHOOL

THE annual clinical meeting of Guy's Hospital Dental School was held on March 1. In the year since the last meeting there have been few sensational advances in dentistry, but it has been a period of steady improvement in methods. The novelty which aroused the greatest interest was an instrument for cavity preparation shown by Mr. W. A. Vale. This is an air-turbine-driven handpiece, capable of speeds up to 50,000 revolutions a minute, which attracted a good deal of attention when it first appeared at the International Dental Congress in Rome last year. Diamond or tungsten-carbide burrs, rotating at high speeds, can cut cavities in teeth rapidly and almost painlessly, and the 'Borden Airotor', as the instrument is called, has many advantages over the conventional electric motor, although at the moment it is rather more costly. At least one patient upon whom the airotor was used said that he was going to ask his own dental surgeon to buy one at the earliest possible opportunity.

A further reminder of the International Dental Congress was the photographic exhibit which the hospital sent to Rome last year. This display included portraits of eminent Guy's dental surgeons of the past, and a series of photographs illustrating the various stages in the career of a dental student.

The dental photographic department, under the able and enthusiastic direction of Mr. A. D. Robinson, who produced this exhibit, showed some of the techniques used in dental photography. Colour photographs of the mouth—not one of the easiest regions of the body to represent satisfactorily—have now been brought to a high degree of technical perfection by Miss Whiteley and her assistants. Mr. Robinson showed a film, entitled *Becoming a Dental Surgeon*, which he made for exhibition to senior schools to give prospective dental surgeons some idea of hospital life.

Towards the end of last year, Prof. M. A. Rushton's department of dental medicine vacated its old and cramped quarters for new and well-equipped rooms in the old pathology block behind the Dental School, and the new premises were on view publicly for the first time on Saturday. The work on which the department is engaged includes an interesting study by Mr. A. C. Kerr on the antibacterial action of human saliva. In the afternoon, Professor Rushton presented his usual annual review of interesting and unusual cases referred to him by dental practitioners; the packed lecture theatre showed what a popular feature of the clinical meeting this lecture has become.

SCOTTISH HOSPITALS ENDOWMENT RESEARCH TRUST

THE Trust issued its first report a year ago.[1] The report for 1955–56 [2] contains a list of those to whom grants have been awarded. The Trust is now prepared to consider paying travelling expenses to enable applicants to attend scientific meetings in the United Kingdom, provided that the expenses are directly connected with a project supported by the Trust.

AMATEUR'S LONDON

AGAINST professionals, such as the police and taxi-drivers, most Londoners show up badly when asked to direct a stranger, say, to the Soane Museum or the Equadorian Embassy. This is not for lack of interest in the topography of London, as anyone will know who has listened in grateful bewilderment to the eager but divergent instructions offered under the general direction of the conductor by a posse of aroused bus passengers once the ice has been broken. But each Londoner tends to have a specialised knowledge of the parish where he lives and/or works. Outside these precincts he is no less vague, indeed often a good deal vaguer, than the intelligent visiting foreigner with a reliable *Baedeker* or *Guide Bleu*. Now he has been offered a guide book [3] of his own by Mr. Colin Hunt, who for over ten years has been coaching taximen for the exacting examination they have to face for their licence. The book contains, among other useful information, 8 maps of the West End and City (17 in. to 1 mile) and over 30 classified lists which alphabetically cover every facet of life from "air transport" to the "University of London", giving not only the address of each institution but also terse instructions on how to locate it. Motorists will study with interest Mr. Hunt's 500 routes which criss-cross London, making due allowance for traffic congestion, from such unlikely points as the Mildmay Mission to the Tavistock Hotel and the Society of Friends Meeting House to Shell-Mex House. It seems curious that this particular book should be published in Edinburgh.

University of Oxford

On March 1 the degree of D.M. was conferred on the following:

G. N. Chandler, *H. M. Lloyd, *Ursula F. Rowlatt.
*In absentia.

University of Birmingham

Dr. D. A. Heath has been appointed lecturer in pathology.

Royal Institute of Public Health and Hygiene

The Harben medal has been awarded to Sir Howard Florey and the Smith award to Dr. Charles White.

1. The Life and Work of Thomas Porter McMurray. By BRYAN MCFARLAND. Liverpool: University Press. 1958. Pp. 12. 5s.

1. See *Lancet*, 1957, i, 676.
2. Scottish Hospitals Endowment Research Trust: Annual Report and Accounts, 1955–56. H.M. Stationery Office, 1958. Pp. 12. 1s.
3. "Here it is" Knowledge of London. Edinburgh: C. J. Consland & Sons. 1958. Pp. 274. 15s. 6d.

Christian Medical Fellowship

ON Wednesday, March 26, at 8.15 P.M. at a meeting of the Christian Medical Fellowship at the Royal Empire Society, Northumberland Avenue, London, W.C.2, Mr. D. MacG. Jackson will speak on moral responsibility in clinical research.

The Wolfenden Report

The Institute for the Study and Treatment of Delinquency is to hold two conferences this year on this report.

The first of these will deal with prostitution and will take place at Bracklesham Bay Hotel, Sussex, from April 18 to 20. The speakers will include Dr. T. C. N. Gibbens and Dr. Edward Glover. Further particulars may be had from the Institute, 8, Bourdon-street, London, W.1.

Carlsberg-Wellcome Travelling Research Fellowships

The directors of the Carlsberg Foundation, in Copenhagen, and the Wellcome Trustees, in London, instituted these fellowships in 1957 to encourage friendly cooperation, on an exchange basis, between Danish and British research-workers in any branch of the natural sciences which has a bearing upon human and animal medicine. One fellowship annually is awarded to a candidate from the United Kingdom for a year's work in Denmark, and one annually to a Danish candidate for a year's work in the United Kingdom.

The stipend may range from £800 to £1200 per annum (or the equivalent sums in Danish kroner) for whole-time research. Travelling and some incidental expenses are provided in addition. It is intended that the second appointments shall be made in respect of the academic year beginning in September, 1958.

Inquiries about these fellowships from candidates in the United Kingdom should be addressed to the scientific secretary of the Trust, 52, Queen Anne Street, London, W.1. There is no form of application, but candidates should submit a full *curriculum vitæ*, together with details of their research proposals and a supporting letter from a senior scientist who is familiar with their work. Completed applications must be submitted before April 30.

Medical Society of London

AT the 178th anniversary dinner the toast of The Society was proposed by Admiral of the Fleet the Earl Mountbatten of Burma. The medical profession, he said, had played an immensely valuable part in the success of the South East Asian campaign. In 1942 before he went out to Burma the annual sickness-rate of the Army was 185%, and for every battle casualty there were 120 sick. With the Prime Minister's agreement a medical advisory division was created consisting of British Army, Navy, and Air Force doctors and an American Army doctor—all specialists in tropical diseases. Thanks to their activities and the wonderful work of the medical services already in SEAC, the sickness-rate had fallen to 50% in 1945. The position had so changed that we were able deliberately to choose unhealthy areas in which to fight—areas in which the Japanese suffered terrible losses from disease but in which we were able to keep our men healthy by our newly developed protective measures. "I know of no other case where medical science played such a vital role in turning victory into defeat as in Burma." He believed that, despite the closure of Naval hospitals, including that of the Royal Naval Hospital, Chatham, which has recently been announced, the Royal Navy still offered as good a career as ever to doctors, with prospects which would probably be better.

Sir Cecil Wakeley, the president, thanking Lord Mountbatten, said that the society was honoured by the presence of one of the key men of the nation. He went on to review the activities of the year, and reported that all the meetings had been well attended. Subjects already discussed ranged from leadership (General Sir Brian Horrocks) to life in a cold climate (H. E. Lewis and J. P. Masterton), and those in prospect included tropical medicine in Great Britain, the early years of anæsthesia, and new lamps for old in cardiology. He expressed the society's warm thanks to the registrar, Mr. P. Minter, and his wife, for their continued help.

In his welcome to The Guests, Mr. E. G. Muir spoke of Lord Mountbatten—First Sea Lord and last Viceroy of India—as a man who had brought to the game of polo the dash of the destroyers and the overall command of the chiefs of staff. Dr. T. F. Fox, who responded to this toast, described the society's annual dinner as always among the most agreeable of London's medical functions.

British European Airways

The medical consultants' panel of this corporation now consists of:

Dr. D. Evan Bedford, consultant cardiologist; Dr. Kenneth Black, consultant physician in diseases of metabolism; Mr. J. D. Cambrook, consultant dental surgeon; Mr. W. D. Coltart, consultant orthopædic surgeon; Dr. James Cyriax, consulting physician in physical medicine; Sir Daniel Davies, consultant physician; Air Vice-Marshal E. D. D. Dickson, consultant otorhinologist (aircrew); Lord Evans, consultant physician; Dr. Keith Jefferson, consultant radiologist; Mr. Rodney Maingot, consultant surgeon; Sir Archibald McIndoe, consultant in plastic surgery; Mr. Wylie McKissock, consultant in neurological surgery; Dr. Swithin Meadows, consultant neurologist; Mr. C. Naunton Morgan, consultant in general surgery; Mr. H. Osmond-Clarke, consultant orthopædic surgeon; Dr. J. D. Robertson, consultant pathologist; Mr. B. W. Rycroft, consultant ophthalmic surgeon; Mr. W. G. Scott-Brown, consultant otorhinologist; Dr. Cedric Shaw, consultant physician in diseases of the chest; Dr. W. A. H. Stevenson, adviser on clinical psychiatry; Dr. E. B. Strauss, consulting physician in psychological medicine; Dr. H. J. Wallace, consultant dermatologist; and Sir Harold Whittingham, consultant in aviation medicine.

The director-general of B.E.A. medical services is Dr. A. Buchanan Barbour.

Sir Hans Krebs has been awarded the gold medal of the Netherlands Society for Physics, Medical Science, and Surgery.

A refresher course for general practitioners is being held at the Southern Hospital, Dartford, Kent, on Fridays, at 2.45 P.M., from April 11 to June 20. Further information may be had from Dr. J. C. Hogarth at the hospital.

On Thursday, March 20, at 5.30 P.M., at the Fountain Hospital, Tooting Grove, London, S.W.17, Dr. J. W. Millen and Dr. D. H. M. Woollam will speak on the experimental production of malformations of the brain.

On Friday, March 21, at 8.45 P.M., at a meeting of the Leicester Christian Medical Association in the Leicester Royal Infirmary, Dr. Edward F. Griffith will speak on psychotherapy and marital disharmony.

A semi-permanent exhibition on moniliasis will be held from March 31 to April 25 at the Institute of Dermatology, Lisle Street, London, W.C.2.

The Ministry of Power has issued the Digest of Pneumoconiosis Statistics for 1956 (obtainable from H.M. Stationery Office. Pp. 20. 3*s*.).

The proceedings of the conference on the Challenge of Mental Deficiency, held by the National Association for Mental Health in Manchester last November, may be had from the Association, 39, Queen Anne Street, London, W.1 (pp. 58. 5*s*.).

The Board of Registration of Medical Auxiliaries have lately added to the registers which they publish a register of audiology technicians and a register of technicians in venereology. Doctors may obtain free copies of these from the Board, B.M.A. House, Tavistock Square, London, W.C.1.

CORRIGENDA: *Essential Fatty Acids, Lipid Metabolism, and Atherosclerosis*.—In the paper by Dr. Laurance W. Kinsell and his colleagues (Feb. 15, p. 334) table IV should have been headed: findings in a woman, aged 49, with no evidence of vascular disease.

Ataralgesia.—We unfortunately introduced a mistake in Dr. Hayward-Butt's letter of Feb. 15. The sentence "It is quite possible that levorphanol will prove as satisfactory as amiphenazole" should have read "It is quite possible that *levallorphan* . . ."

Appointments

BAIRD, I. McL., M.D. St. And., M.R.C.P.: part-time consultant physician, Barnsley group of hospitals.
BAKER, C. H. J., M.R.C.S., D.P.H.: school M.O. and assistant M.O.H., Exeter.
DAVIES, D. K. L., M.B. Wales, D.M.R.D.: consultant radiologist, Cardiff H.M.C. group.
KINDER, C. H., M.CHIR. Cantab., F.R.C.S.: assistant surgeon, genito-urinary department, Guy's Hospital, London.
MEEK, J. C., M.B. Glasg., D.M.R.: consultant radiologist, Newport H.M.C. group.
MURRAY, C. J. B., M.S. Lond., F.R.C.S.: consultant surgeon, Royal Masonic Hospital, London.
SIEGLER, JOSEPH, M.B. Lond., F.R.C.S., D.L.O.: part-time consultant otorhinolaryngologist, Liverpool Ear, Nose and Throat Infirmary, Clatterbridge Hospital, and Aintree Hospital.
TUCKWELL, E. G., M.CH. Oxon., F.R.C.S.: consultant surgeon, Royal Masonic Hospital, London.
WALTERS, GLYNDWR, M.D. Brist., M.R.C.P.: consultant pathologist, Wolverhampton group of hospitals.

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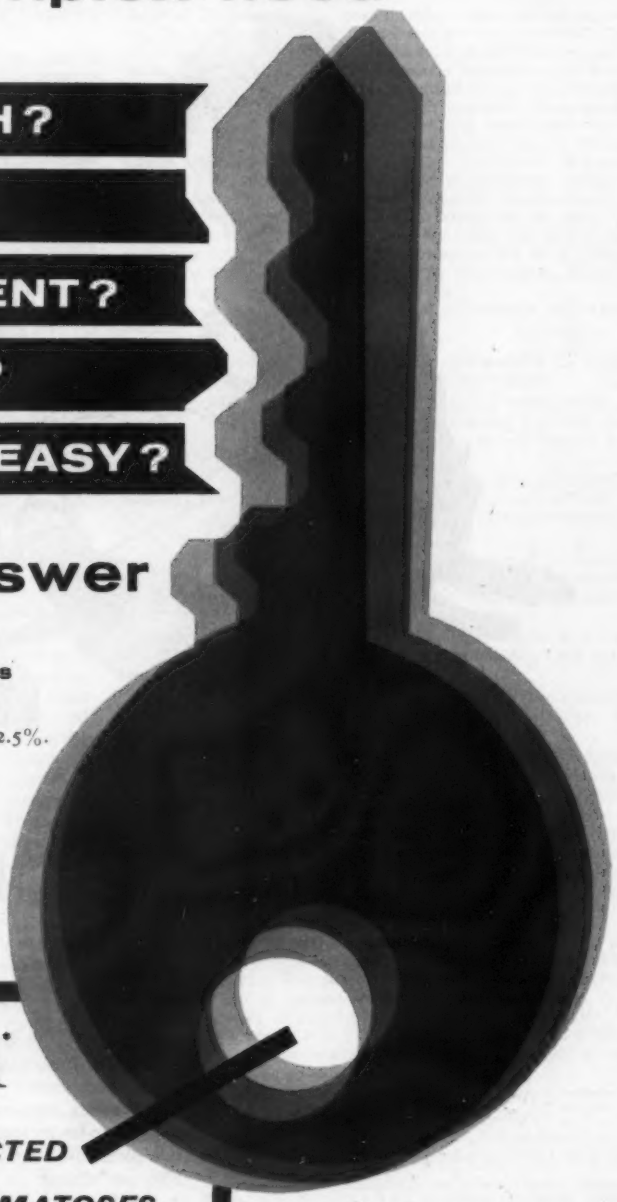

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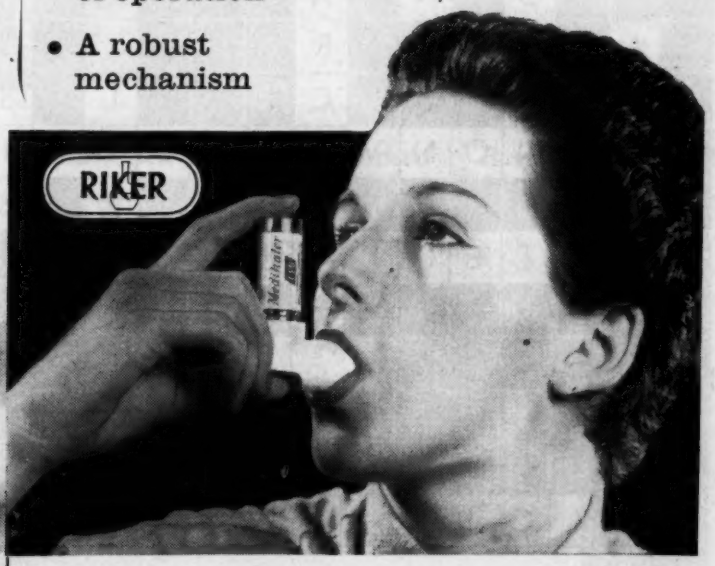

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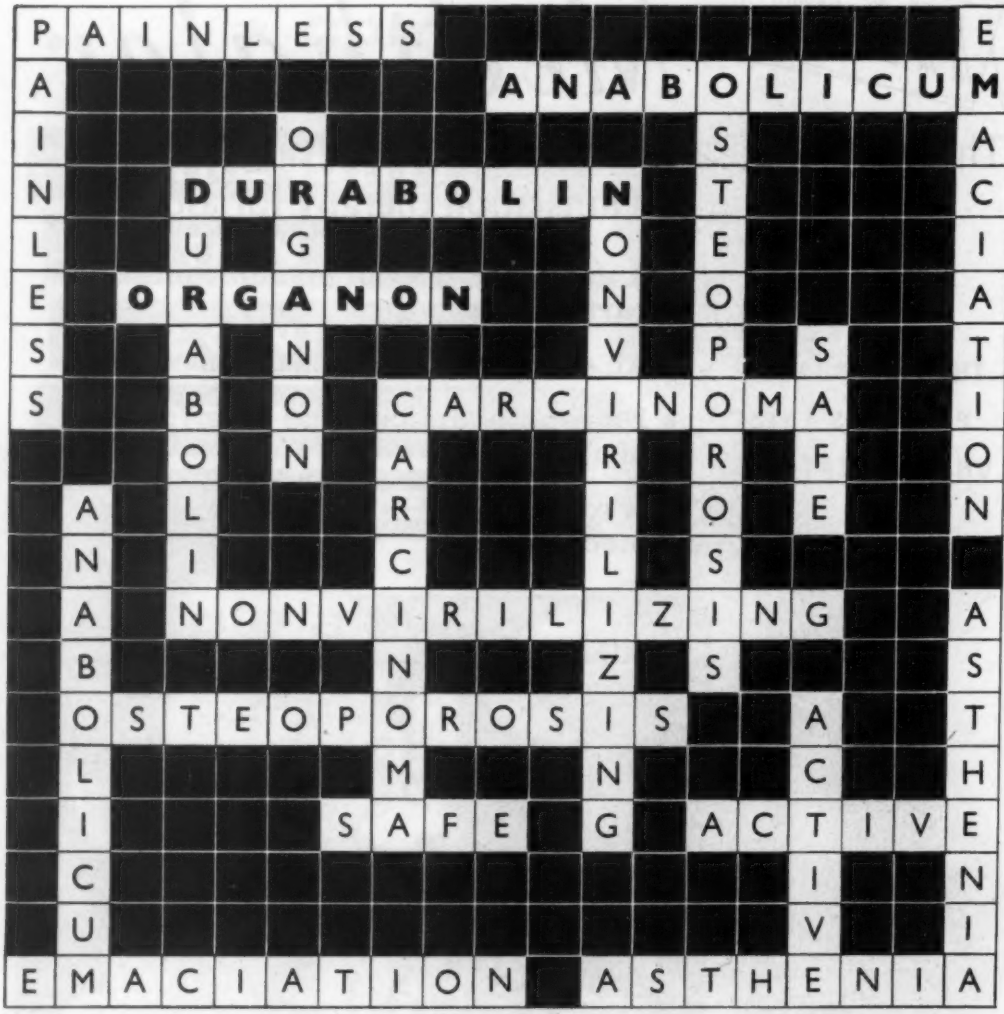

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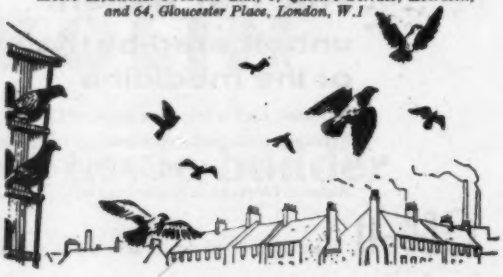

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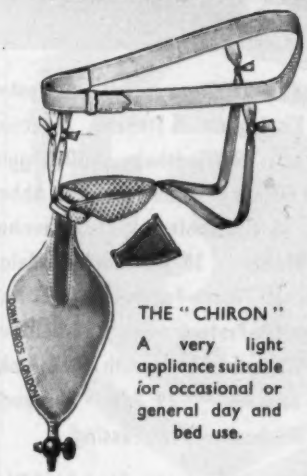

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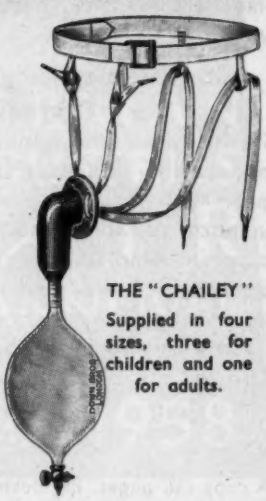

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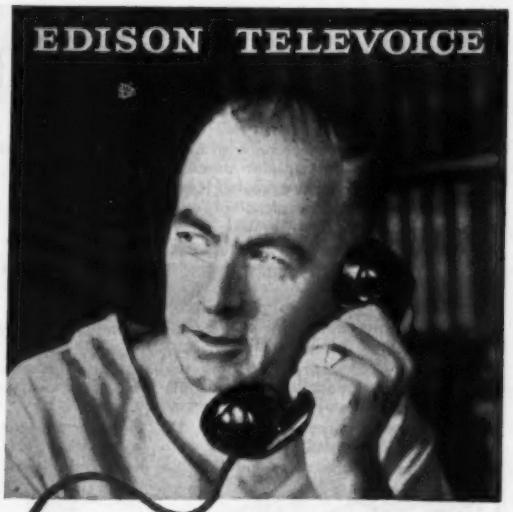

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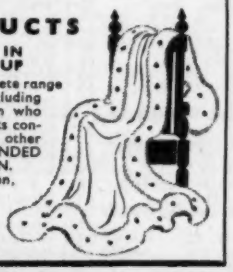

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MOULTON PARK. Two miles from the Main Hospital there are several branch establishments and villas situated in a park and farm of 650 acres. Milk, meat, fruit, and vegetables are supplied to the Hospital from the farm, gardens, and orchards of Moulton Park. Occupational therapy is a feature of this branch, and patients are given every facility for occupying themselves in farming, gardening, and fruit growing.

BRYN-Y-NEUADD HALL. The seaside home of St. Andrew's Hospital is beautifully situated in a park of 330 acres, at Llanfairfechan, amidst the finest scenery in North Wales. On the North-West side of the Estate a mile of sea coast forms the boundary. Patients may visit this branch for a short seaside change or for longer periods. The Hospital has its own private bathing house on the seashore. There is trout-fishing in the park.

For terms and further particulars apply to the Medical Superintendent (TELEPHONE: Northampton 4354, 3 lines), who can be seen in London by appointment.

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The Terms and Conditions of Service of Hospital Medical and Dental Staff apply to all N.H.S. hospital posts we advertise, unless otherwise stated. Canvassing disqualifies, but candidates may normally visit the hospital by appointment.

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A COURSE OF 12 SUBSCRIPTION LECTURES in ADVANCED SURGERY suitable for candidates for the Final F.R.C.S. will be delivered in the Hall, Black Friars Lane, Queen Victoria-street, E.C.4, at 5 P.M. and 6.15 P.M. as follows :—

Thursday, 27th March		
5 P.M.	Non-malignant Diseases of the Colon	C. NAUNTON MORGAN, Esq., F.R.C.S.
6.15 P.M.	Genito-urinary Tuberculosis	A. W. BADENOCH, Esq., M.D., CH.M., F.R.C.S.
Friday, 28th March		
5 P.M.	Endocrine Therapy in Surgery	Prof. Sir CHARLES DODDS, M.V.O., M.D., F.R.C.P., F.R.S.
6.15 P.M.	Splenectomy	RODNEY MAINGOT, Esq., F.R.C.S.
Monday, 31st March		
5 P.M.	Carcinoma of the Thyroid	R. VAUGHAN HUDSON, Esq., F.R.C.S.
6.15 P.M.	Carcinoma of the Breast	R. S. HANDLEY, Esq., O.B.E., F.R.C.S.
Tuesday, 1st April		
5 P.M.	Hæmatemesis	Prof. IAN AIRD, CH.M., F.R.C.S.
6.15 P.M.	Gallstones	Sir CECIL WAKELEY, BT., K.B.E., C.B., F.R.C.S.
Wednesday, 2nd April		
5 P.M.	Malignant Melanoma	Sir STANFORD CADE, K.B.E., C.B., F.R.C.S.
6.15 P.M.	The Surgical Treatment of Pulmonary Tuberculosis	VERNON C. THOMPSON, Esq., F.R.C.S.
Thursday, 3rd April		
5 P.M.	Compound Fractures of the Tibia and Fibula	W. ALEXANDER LAW, Esq., O.B.E., M.D., F.R.C.S.
6.15 P.M.	Pott's Disease of the Spine	W. D. COLTART, Esq., F.R.C.S.

Tea will be served between each 2 lectures.
Fee for the whole course £5 5s. Single lecture 10s. 6d.
Tickets may be obtained from the Registrar.

THE ERNEST AND MINNIE DAWSON CANCER TRUST

A COMPETITION FOR GENERAL MEDICAL PRACTITIONERS

The purpose of the Ernest and Minnie Dawson Cancer Trust, which came into being in 1955, is to arrange competitions between selected general medical practitioners and to give big financial prizes to such practitioners who from time to time make what is considered to be the most valuable contribution to the early diagnosis, prevention and treatment of cancer and to knowledge of its causes.

The second competition, which will close on the 1ST MAY, 1959, will take the form of a thesis on cancer. The subject matter is at the discretion of the entrant and may relate to cancer in various sites or cancer of one organ; it must also lay emphasis on one or more of the following : (*a*) early diagnosis ; (*b*) causes ; (*c*) prevention ; and (*d*) treatment. All entries must contain original thought and observation, and be the result of personal endeavour.

The competition is open to doctors mainly engaged in general practice who practise and/or reside in Lancashire or Yorkshire; and the maximum prizes offered are £1500 (first) and £500 (second), subject to the merit of the entries submitted.

Entry forms and detailed conditions of entry may be obtained from the Clerk to the Trust, the Ernest and Minnie Dawson Cancer Trust, 89A, Fishergate Hill, Preston, Lancs.

E. PEARSON, Clerk to the Trust.

INSTITUTE OF DISEASES OF THE CHEST

CONSULTANTS' CONFERENCE

A Consultants' Conference will be held at the Institute from 7TH to 11TH JULY.

7th and 8th July : Symposium on "Cardio-Respiratory Resuscitation".

9th July : Informal demonstrations.

10th and 11th July: Symposium on "The Chemotherapy of Tuberculosis".

Further information and detailed programmes can be obtained from the Dean, Institute of Diseases of the Chest, Brompton Hospital, London, S.W.3. Application may be made to attend for the whole week or for either of the 2 symposia. The conference is intended for those of Consultant or equivalent status.

THE INSTITUTE OF ACCIDENT SURGERY

A COURSE in the Acute Treatment of Injuries will be held at the Birmingham Accident Hospital, 5TH–9TH MAY, 1958. Fees, including lunch and tea, will be 8 guineas.

Applications and inquiries from the Secretary, The Institute of Accident Surgery, Birmingham Accident Hospital, Bath-row, Birmingham, 15.

ROYAL COLLEGE OF SURGEONS OF ENGLAND. DEPARTMENT OF PHYSIOLOGY. Applications are requested for the post of H. N. SMITH RESEARCH FELLOW to work in the general field of wound healing. Salary range £1000–£1500 p.a., according to qualifications and experience. F.S.S.U.

For further particulars apply to the Professor of Physiology, Royal College of Surgeons, Lincoln's Inn-fields, London, W.C.2.

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WALTER MYER AND EVERETT DUTTON CHAIR OF PARASITOLOGY AND ENTOMOLOGY

The Council of the University invites applications for the Walter Myer and Everett Dutton Chair of Parasitology and Entomology. The appointment will date from 1ST OCTOBER, 1958.

Further particulars may be obtained from the undersigned by whom 20 copies of applications (1 in the case of overseas candidates) should be received not later than 26th April, 1958.

STANLEY DUMBELL, Registrar.

POSTGRADUATE MEDICAL SCHOOL. Applications are invited for the post of ASSISTANT LECTURER IN BACTERIOLOGY vacant on 1st April. Duties involve teaching and supervision of routine work. Opportunity for research. Salary range £1250–£100–£1650.

Applications (5 copies), with names of 2 referees, to the Dean, Postgraduate Medical School, Ducane-road, W.12, from whom further information can be obtained.

FARNBOROUGH HOSPITAL. Children's Department. Applications are invited for an appointment as RESEARCH MEDICAL OFFICER for a therapeutic trial. Salary at the rate of £900 p.a. if whole-time.

Inquiries to the Secretary, Children's Department, Farnborough Hospital, Kent. (Tel. Farn. 53333, Ext. 279.)

THE UNIVERSITY OF LEEDS. Department of Pathology. Applications are invited from graduates in medicine or science (if the latter, preferably with a Ph.D. in one of the medical sciences) for appointment to the LYONS FELLOWSHIP FOR MULTIPLE SCLEROSIS AND ALLIED NERVOUS DISEASES of the annual value of £1250 rising by £100 a year; the appointment will be for 1 year in the first instance, renewable for 2 further years. Under the direction of the Professor of Pathology the Fellow will take part in a combined programme of research on the biology of myelin and the experimental pathology of the demyelinating diseases.

Applications (3 copies), stating date of birth, qualifications and experience, together with the names of 3 referees, should reach the Registrar, The University, Leeds, 2 (from whom further particulars may be obtained), not later than 14th April, 1958.

UNIVERSITY OF LEEDS. UNITED LEEDS HOSPITALS. Applications are invited for the post of SENIOR REGISTRAR AND TUTOR IN PSYCHIATRY. The successful candidate will be a member of the University Department of Psychiatry and the duties will include work at the General Infirmary at Leeds with which the University Department is associated and such other duties as may be assigned to him by the Head of the University Department.

Applications (3 copies), stating date of birth, qualifications and details of present and previous appointments with dates, and experience of teaching, together with the names of 3 referees, should reach the Registrar, The University, Leeds, 2 (from whom further particulars may be obtained), not later than 14th April, 1958.

UNIVERSITY OF ST. ANDREWS. The University Court of the University of St. Andrews invites applications for either an ASSISTANTSHIP IN PHYSIOLOGY, or an appointment as DEMONSTRATOR IN HUMAN PHYSIOLOGY, in the Department of Physiology and Biochemistry, St. Salvator's College, St. Andrews.

The Assistantship will be for a period of 3 years, and the salary £900–£100–£1200 for medically qualified persons; if not medically qualified, £700–£50–£850. F.S.S.U. and family allowance benefits.

Applications (6 copies), together with the names of 3 referees, should be lodged with the undersigned not later than 12th April, 1958.

The appointment as Demonstrator, for which a medical qualification is essential, will be for 1 year only, at a salary of £500. The primary duties will be to assist in the teaching of human physiology and biochemistry to medical students, and the post offers facilities for study for a higher qualification in Medicine or Surgery.

Further particulars can be obtained from the Professor of Physiology, Bute Medical Buildings, St. Andrews.

D. M. DEVINE, Joint Clerk to the University Court.

College Gate, St. Andrews.

UNIVERSITY COLLEGE, Ibadan, Nigeria. Applications are invited for:—

CHAIR OF PATHOLOGY.
CHAIR OF SURGERY.

Duties consist of research and teaching of students along lines of London curriculum for M.B., B.S., and clinical work in the case of surgery. The Departments are in the new University College Hospital. Appointees will be offered honorary consultantships by the Hospital. Salary £3000 p.a.; child, car and outfit allowances. Part-furnished accommodation at rent not exceeding 7·7 % of salary. Passages for appointee, wife and up to 3 children below age of 11 years, on appointment, overseas leave and termination. F.S.S.U.

Detailed applications (12 copies), naming 3 referees, by 16th April, 1958, to Secretary, Senate Committee on Colleges Overseas in Special Relation, University of London, Senate House, London, W.C.1, who has further particulars.

UNIVERSITY COLLEGE, Ibadan, Nigeria. Applications are invited for a LECTURESHIP IN OBSTETRICS AND GYNÆCOLOGY from candidates with M.R.C.O.G. Initial appointment 3 years. Honorary appointment to University College Hospital. Salary scale: £1700–£100–£2100 p.a. Child, car and outfit allowances. Part furnished accommodation at rent not exceeding 7·7 % of salary. Passages for appointee, wife and up to 3 children below age of 11 years, on appointment, overseas leave and termination. F.S.S.U.

Detailed applications (10 copies), naming 3 referees, by 21st April, 1958, to Secretary, Senate Committee on Colleges Overseas in Special Relation, University of London, Senate House, London, W.C.1, from whom further particulars may be obtained.

Hospital Services: Senior Appointments

NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD.
(1) CONSULTANT SURGEON, 3 half-days a week, Acton Hospital, Gunnersbury-lane, Acton, W.3. (84 Beds.)
Applications before 21st April, 1958.
(2) CONSULTANT HOMŒOPATHIC PHYSICIAN, 2 half-days a week, Royal London Homœopathic Hospital, Great Ormond-street, W.C.1. (183 Beds.) Post vacant 1st August, 1958.
Applications before 25th April, 1958.
Hospitals may be visited by direct appointment.
Application forms obtainable from and returnable to the Secretary, North West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1.

ROYAL MARSDEN HOSPITAL, London, S.W.3. Applications are invited for the post of CONSULTANT RADIOTHERAPIST (full-time or maximum part-time) in the Department of Radiotherapy at the Royal Marsden Hospital and Institute of Cancer Research, Royal Cancer Hospital. Higher qualification (F.R.C.S., M.R.C.P., F.F.R.) expected. Special interest in urology and radioactive isotope therapy desirable but not essential.
Applications (12 copies), quoting age, education, experience, and giving names of 3 referees, to reach the House Governor, Royal Marsden Hospital, Fulham-road, London, S.W.3, by 12th April, 1958.

ST. MARY'S HOSPITAL, Paddington, W.2. Applications are invited from practitioners holding a higher medical qualification for the post of CONSULTANT IN CHARGE of the Clinic for Allergic Disorders (Wright Fleming Institute of Microbiology) for 7 notional half-days per week. The successful candidate will be required to have considerable experience in the treatment of allergic disorders and will be expected to take up his duties on 1st July, 1958. He will be required to devote the remainder of his time to research work for which he will be paid by the Wright Fleming Institute.
Applications (12 copies), stating nationality, date of birth, permanent address, qualifications with dates, details and National Health Service gradings of previous and present appointments, together with the names and addresses of 3 referees, should be sent not later than 26th April, 1958, to the House Governor, St. Mary's Hospital, London, W.2, from whom further information may be obtained.

ST. THOMAS'S HOSPITAL, London, S.E.1. South West METROPOLITAN REGIONAL HOSPITAL BOARD. OBSTETRICIAN AND GYNÆCOLOGIST (joint appointments). 6 sessions per week, of which 3 will be at Lambeth Hospital. Consultant status and membership of the Hospitals' Medical Committees.
Applications (12 copies), including names and addresses of 3 referees, to the Clerk of the Governors, St. Thomas's Hospital, by 28th March, 1958.

WHITTINGTON HOSPITAL, London, N.19. Locum Tenens ASSISTANT ORTHOPÆDIC SURGEON (Senior Hospital Medical Officer grade), non-resident, required immediately for 3 months in the first instance.
Write or call Medical Superintendent (ARChway 3070, extension 440).

BIRMINGHAM REGIONAL HOSPITAL BOARD. Whole-time Locum Tenens CONSULTANT SURGEON, Dudley Road Hospital, Birmingham (246 surgical beds). Vacant immediately. Wide experience specialty and higher qualification required.
Apply immediately to Secretary, 10, Augustus-road, Birmingham, 15.

LEEDS REGIONAL HOSPITAL BOARD. Whole-time Locum ASSISTANT PSYCHIATRIST (Senior Hospital Medical Officer scale) for duties at Menston Hospital, near Leeds, and associated clinics at Bradford, Leeds and Keighley. Applicants should hold the D.P.M. or other equivalent qualifications. The post is now vacant and appointment will be for a minimum of 3 months. Accommodation is available for a single person.
Applications, stating age, qualifications and details of appointments held, showing dates, with names and addresses of 3 referees, to the Secretary, Park-parade, Harrogate, by 19th March, 1958.

LIVERPOOL REGIONAL HOSPITAL BOARD. Victoria CENTRAL HOSPITAL, WALLASEY. Applications are invited for the post of Part-time ASSISTANT OPHTHALMOLOGIST (Senior Hospital Medical Officer) giving 1 notional half-day at the above Hospital. The successful applicant will work under the direction of the Consultant Ophthalmologist.
Forms of application from Dr. T. Lloyd Hughes, Senior Administrative Medical Officer, Liverpool Regional Hospital Board, 19, James-street, Liverpool, 2, to be returned not later than 5th April, 1958.
VINCENT COLLINGE, Secretary to the Board.

SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time ASSISTANT RADIOLOGIST for Leicester Royal Infirmary and Leicester General Hospital. The successful candidate will work under the direction of the Consultant Radiologist in Charge and will be required to reside within 10 miles of Leicester Royal Infirmary. Candidates should possess a diploma in Radiology. Salary scale £1653 15s.–£52 10s.–£2126 5s. p.a.
Application forms and further details from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield. Forms to be returned by 14th April, 1958.

SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time SENIOR CASUALTY OFFICER required at the Mansfield and District General Hospital. Married accommodation available at Victoria Hospital, Mansfield. Salary scale £1653 15s.–£52 10s.–£2126 5s. p.a. Tenure for a period not exceeding 4 years.
Application forms and further details from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield. Forms to be returned by 14th April, 1958.

SCOTLAND. EASTERN REGIONAL HOSPITAL BOARD. DUNDEE ROYAL MENTAL HOSPITAL (GOWRIE HOUSE) and MARYFIELD HOSPITAL, DUNDEE. Applications are invited for a whole-time appointment of PSYCHIATRIST (Consultant) to the Dundee Mental Hospitals. The duties will be primarily in Dundee Royal Mental Hospital (100 Beds for acute mental illness) and in the Psychiatric Ward and Outpatient Clinic at Maryfield (general and teaching) Hospital, Dundee (370 Beds). Both Hospitals are associated with the University of St. Andrews. Salary and conditions of service in accordance with National Agreement.
Further particulars and forms of application from the Secretary to the Board, 430, Blackness-road, Dundee, with whom applications must be lodged not later than 5th April, 1958.

SCOTLAND. WESTERN REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of CONSULTANT PHYSICIAN in charge of wards at the Victoria Infirmary, Glasgow. The appointment is part-time on the basis of 7 notional half-days per week.
Applications (16 copies), stating date of birth, qualifications, experience, present appointment, and the names of 3 referees, to reach the Secretary, Western Regional Hospital Board, 64, West Regent-street, Glasgow, C.2, not later than 30 days after the publication of this advertisement.

NORTHERN IRELAND HOSPITALS AUTHORITY. Locum Tenens for Consultants and Specialists. Applications are invited for Whole-time LOCUM TENENS posts in Anæsthetics, General Medicine, Radiology, and Orthopædic Surgery at Hospitals in various parts of Northern Ireland during the months June to September, 1958. Remuneration will be at the rate of £34 14s. 6d. per week or, if the locum is of Consultant status, at the rate of £52 10s. per week.
Applications to be made on a form obtainable (with further particulars) from the Secretary, Northern Ireland Hospitals Authority, 44/46, Queen-street, Belfast, and to be returned as soon as possible.

TASMANIA. LAUNCESTON GENERAL HOSPITAL, LAUNCESTON. Applications are invited from qualified medical practitioners for the position of DEPUTY SUPERINTENDENT Salary £A2000 p.a. If the applicant is in possession of higher qualifications in medicine, his commencing salary will be £A2250 p.a. An assisted passage can be arranged through the Immigration Department.
Applications to be addressed to the General Superintendent from whom any further particulars regarding appointment may be obtained. B. W. GRIFFITHS, Secretary.

Hospital Services: Junior Appointments

BOLINGBROKE HOSPITAL, Wandsworth Common, S.W.11. HOUSE PHYSICIAN (resident), vacant 31st March, 1958. Open to registered practitioners and pre-registration candidates.
Apply Hospital Secretary, enclosing copies of 3 recent testimonials, by 17th March, 1958.

BRITISH HOSPITAL FOR MOTHERS AND BABIES, Samuel-street, Woolwich, S.E.18. SENIOR HOUSE OFFICER (obstetrics) vacant 18th April. Recognised for D.Obst.R.C.O.G. and M.R.C.O.G.
Apply to Group Secretary, Memorial Hospital, Woolwich, S.E.18.

CHILDREN'S HOSPITAL, Sydenham, S.E.26. House OFFICER (medicine and surgery) required 29th April. Recognised for D.C.H.
Apply, naming 2 referees, to the Administrative Officer, by 22nd March.

DREADNOUGHT SEAMEN'S HOSPITAL, Greenwich, S.E.10. HOUSE SURGEON (pre-registration) required immediately.
Applications, stating age, nationality, qualifications and experience and giving the names of 3 recent referees, should be sent to the Secretary at the above address not later than 22nd March.

DULWICH HOSPITAL, East Dulwich-grove, S.E.22. HOUSE SURGEON (general surgical duties). Recognised pre-registration post.
Applications, with copy testimonials or names of 2 referees, to Group Secretary, Camberwell Hospital Management Committee, Dulwich Hospital, East Dulwich-grove, S.E.22.

FULHAM HOSPITAL, St. Dunstan's-road, Hammersmith, W.6. Applications invited for appointment as ORTHOPÆDIC REGISTRAR (full-time, non-resident). Post vacant 12th April, 1958. Wide variety of orthopædics and traumatic surgery is handled in the Department. Post recognised for F.R.C.S. Candidates may visit Hospital by arrangement with Hospital Secretary.
Applications (5 copies) to be submitted by 28th March, 1958, on forms obtainable from, and returnable to, Group Secretary, 5, Collingham-gardens, London, S.W.5. (L.152).

GERMAN HOSPITAL, London, E.8. (General—157 Beds.) Applications for the 12 months' resident appointment, vacant 27th March, of SENIOR HOUSE OFFICER (general surgery), should be sent to Group Secretary, Hackney Hospital, E.9, by 24th March, quoting GH/SHO.

GROUP PATHOLOGICAL LABORATORY, ST. MARY ABBOTS HOSPITAL, Marloes-road, Kensington, W.8. FULHAM AND KENSINGTON AND CHELSEA HOSPITAL MANAGEMENT COMMITTEES. Applications are invited for appointment as REGISTRAR (pathology), vacant 4th June, 1958. Candidates will be required to work at the Group Laboratory and as required at any other hospital in either of the 2 groups. Candidates may visit the Laboratory by arrangement with the Director of Pathology.
Applications (5 copies) to be submitted by 28th March, 1958, on forms obtainable from, and returnable to the Group Secretary, 5, Collingham-gardens, London, S.W.5. (L.155.)

HAMMERSMITH HOSPITAL AND POSTGRADUATE MEDICAL SCHOOL, Ducane-road, London, W.12. Whole-time NON-RESIDENT REGISTRAR required for Radiodiagnostic Department as soon as possible.

Applications, stating age, qualifications, experience, names 2 referees, to Secretary, Board of Governors, The Hammersmith, West London and St. Mark's Hospitals, Ducane-road, W.12, by 24th March.

HAMMERSMITH HOSPITAL AND POSTGRADUATE MEDICAL SCHOOL, Ducane-road, London, W.12. Joint appointment with the NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Whole-time REGISTRAR (orthopædic) required. Post vacant now. Appointment tenable firstly at Heatherwood Hospital, Ascot (resident if required), studying long-term orthopædic surgery, transferring to Hammersmith Hospital and the Postgraduate Medical School (non-resident) on 1st August, 1958, studying orthopædic and traumatic surgery.

Applications, stating age, qualifications, experience, names 2 referees, to Secretary, Board of Governors, The Hammersmith, West London and St. Mark's Hospitals, Ducane-road, London, W.12, by 24th March.

HAMPSTEAD GENERAL HOSPITAL, Haverstock-hill, N.W.3. (ROYAL FREE HOSPITAL GROUP.) Applications are invited for the post of Locum HOUSE PHYSICIAN (pre-registration) for the period 1st April to 14th June, 1958.

Application forms may be obtained from the Secretary, to whom they should be returned by 20th March, 1958.

HAMPSTEAD GENERAL HOSPITAL, Haverstock-hill, N.W.3. (ROYAL FREE HOSPITAL GROUP.) Applications are invited for the post of Locum HOUSE SURGEON (pre-registration) for the period 25th March to 14th June, 1958.

Application forms may be obtained from the Secretary, to whom they should be returned by 20th March, 1958.

LAMBETH HOSPITAL, Brook-drive, S.E.11. Applications are invited from pre-registration and registered medical practitioners for the appointment of RESIDENT HOUSE SURGEON in the Obstetric and Gynæcological Unit. Appointment for 6 months from 1st May, 1958. It would be a convenience if the successful candidate could carry out a fortnight's Locum duty starting 17th April, 1958. Recognised for M.R.C.O.G. and D.Obst.R.C.O.G.

Application forms from the Secretary; self-addressed envelope should be enclosed.

LONDON HOSPITAL, Whitechapel, E.1. Applications are invited for the post of REGISTRAR or SENIOR REGISTRAR (according to experience) in the Department of Neurosurgery. A higher surgical qualification is essential.

Applications (12 copies), giving the names and addresses of 3 referees, should be received by the undersigned by 25th March, 1958. H. BRIERLEY, House Governor.

MARIE CURIE HOSPITAL, 66, Fitzjohn's-avenue, Hampstead, N.W.3. HAREFIELD AND NORTHWOOD GROUP HOSPITAL MANAGEMENT COMMITTEE. RESIDENT MEDICAL OFFICER (House Officer grade) required mid-April.

Applications, with copies of testimonials, to the Administrative Officer by 22nd March, 1958.

MOORFIELDS EYE HOSPITAL (High Holborn Branch), London, W.C.1. Applications are invited from Male Practitioners for the non-resident post of CASUALTY OFFICER (Registrar grade). The successful candidate will be required to take up his duties on 1st June, 1958. If recommended by the Medical Committee, he will be eligible for appointment from 1st December, 1958, to the posts of Third, Second and First Resident Surgical Officer (Registrar grade) consecutively for a period of 6 months in each case, making a total period of service of 2 years. Experience in ophthalmology is essential.

Forms of application are obtainable from the undersigned to whom they should be returned, with not more than 3 testimonials, by 18th April, 1958. G. DE B. PLEYDELL, Deputy House Governor.

NORTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD.

MEDICAL REGISTRAR (resident). Chelmsford and Essex and St. John's Hospitals, Chelmsford, Essex. Available for 1 year only from April.

MEDICAL REGISTRAR (resident). St. Margaret's Hospital, Epping, Essex.

REGISTRAR in General Surgery and Orthopædics (non-resident). Metropolitan Hospital, London, E.8. F.R.C.S. desirable.

SURGICAL REGISTRAR (non-resident). Prince of Wales's General Hospital, Tottenham, N.15, and other hospitals in the Tottenham Group. Recognised for F.R.C.S.

Appointments subject to review after 1 year.

Application forms from Secretary, 11A, Portland-place, W.1, to be returned by 29th March, 1958.

NORTH MIDDLESEX HOSPITAL, London, N.18. Senior HOUSE OFFICER for Thoracic Surgical Unit, resident, required for 24th March. 6 months' appointment, with possible extension to 1 year. The post, which is recognised for F.R.C.S., offers experience in all types of tuberculous and non-tuberculous thoracic surgery.

Applications, stating age, nationality, qualifications, experience, with copies of recent testimonials and/or names of 2 referees, to Hospital Secretary.

NORTH MIDDLESEX HOSPITAL, London, N.18. Obstetric AND GYNÆCOLOGICAL HOUSE SURGEONS, resident, required for 1st May:—

(*a*) Post-registration.

(*b*) Pre-registration (second post).

Posts recognised by R.C.O.G. for Diploma, and as combined posts for Membership. Candidates must have held house appointments in either medicine or surgery. Large obstetric and gynæcological department.

Applications (in own handwriting), stating age, nationality, qualifications, experience, with copies of recent testimonials, to Hospital Secretary, by 26th March.

NORTH MIDDLESEX HOSPITAL, London, N.18. House PHYSICIAN, post-registration, resident, required for 1st May. General medicine.

Applications (in own handwriting), stating age, nationality, qualifications, experience, with copies of recent testimonials, to Hospital Secretary, by 26th March.

NORTH MIDDLESEX HOSPITAL, London, N.18. Senior HOUSE OFFICER in Anæsthetics, resident, required, for 14th April. Candidates should have had previous anæsthetic experience. Hospital recognised for training for D.A. and F.F.A. R.C.S. Post offers wide experience in anæsthetics. Appointment is for 6 months in the first instance with possible extension to 1 year.

Applications, stating age, nationality, qualifications, experience, with copies of recent testimonials and/or names of 2 referees, to Hospital Secretary, by 19th March.

QUEEN MARY'S HOSPITAL FOR THE EAST END, Stratford, E.15. PÆDIATRIC HOUSE PHSYCIAN (Male or Female, House Officer, third post). Duties will include some work in related departments (e.g., Diabetic Clinic, &c.). 6 months commencing 13th April, 1958. Post recognised for D.C.H.

Applications, with the names of 3 referees, to Hospital Secretary by 22nd March, 1958.

QUEEN MARY'S HOSPITAL FOR THE EAST END, Stratford, E.15. SENIOR OBSTETRIC HOUSE SURGEON (Male or Female, Senior House Officer grade). 6 months commencing 1st May, 1958. Post recognised for M.R.C.O.G.

Applications with the names of 3 referees to Group Secretary, West Ham Group Hospital Management Committee, Stratford, E.15, by 22nd March, 1958.

QUEEN MARY'S HOSPITAL FOR THE EAST END, Stratford, E.15. JUNIOR CASUALTY OFFICER (House Officer, third post) required for 6 months commencing 10th April, 1958.

Applications, with the names of 3 referees, to Hospital Secretary by 22nd March, 1958.

QUEEN MARY'S HOSPITAL FOR THE EAST END, Stratford, E.15. OBSTETRIC HOUSE SURGEON (Male or Female, House Officer, third post). 6 months commencing 1st May, 1958. Successful candidate may be eligible for appointment as Senior Obstetric House Surgeon (Senior House Officer grade) for the following 6 months. Post recognised for M.R.C.O.G.

Applications, with the names of 3 referees, to Hospital Secretary by 22nd March, 1958.

REGIONAL NEUROSURGICAL CENTRE (66 Beds), Brook General Hospital, Shooters Hill-road, S.E.18. SENIOR HOUSE OFFICER (neurosurgery). Post recognised for F.R.C.S. and D.P.M., and provides excellent opportunity for training in neurology.

Apply to Group Secretary, Memorial Hospital, Woolwich, S.E.18.

ROYAL FREE HOSPITAL. Applications are invited from registered medical practitioners for the post of RESIDENT PATHOLOGIST (Senior House Officer). The post is for 1 year from 1st April, 1958. Salary and conditions of service as laid down by the Ministry of Health.

Application forms may be obtained from the Secretary, Royal Free Hospital, Gray's Inn-road, London, W.C.1, to whom they should be returned not later than 29th March, 1958.

ROYAL NATIONAL THROAT, NOSE AND EAR HOSPITAL, Gray's Inn-road, W.C.1, and Golden-square, W.1, in association with the INSTITUTE OF LARYNGOLOGY AND OTOLOGY. Applications are invited for 1 post of REGISTRAR and 1 post of SENIOR HOUSE OFFICER. The appointments will be in accordance with National Health Service terms and conditions of service, and for initial periods of 12 and 6 months respectively.

Applications, giving full information and the names of 2 referees, should be sent to the House Governor by 5th April.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for an appointment as Whole-time REGISTRAR in General Surgery to fill a vacancy in the approved trainee establishment at the Lewisham Group of hospitals. The appointment will be in accordance with the terms and conditions of service of hospital medical and dental staff (England and Wales), and will be for 1 year in the first instance.

Applications, giving particulars of age, qualifications and experience with relevant dates, together with the names and addresses of 2 referees, to be sent to the Secretary, Registrars Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, London, W.1, not later than 29th March, 1958.

SOUTH WESTERN HOSPITAL, Landor-road, Stockwell, S.W.9. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited from registered medical practitioners for the post of MEDICAL REGISTRAR with duties mainly in the Acute Medical Unit (32 Beds), which is under the control of the Consultant Physician from Lambeth Hospital. The appointment, which will become vacant on 4th June, 1958, is normally for 2 years but is subject to annual review. Candidates may visit the Hospital by arrangement.

Forms of application obtainable from Group Secretary, Lambeth Group Hospital Management Committee, Renfrew-road, S.E.11, should be returned by 29th March, 1958.

SOUTH WESTERN HOSPITAL, Landor-road, S.W.9. Applications are invited from Women candidates for the post of HOUSE SURGEON (pre-registration). Vacant now. Duties include general surgery, and the successful candidate will also be required to relieve the House Surgeon at the Annie McCall Maternity Hospital.

Application forms, from the Hospital Secretary, to be returned immediately.

ST. JAMES' HOSPITAL, Balham, London, S.W.12. SENIOR HOUSE OFFICER (orthopædic and trauma). Post recognised for F.R.C.S. Vacant now.

Applications, stating age, qualifications, experience and names of 2 referees, to Group Secretary, Wandsworth Hospital Group, at above address, immediately.

ST. ANDREW'S HOSPITAL, Bow, E.3. House Physician required. Recognised pre-registration post.

Applications, with copy of at least 1 testimonial, to the Hospital Secretary immediately.

ST. ANDREW'S HOSPITAL, Devons-road, Bow, E.3. House SURGEON required, for duties in the Ophthalmic Department and Casualty Unit. Applicants must be fully registered.

Applications, with copy of at least 1 testimonial, should be sent to the Hospital Secretary immediately.

ST. LEONARD'S HOSPITAL, Nuttall-street, London, N.1. Applications are invited from registered or provisionally registered medical practitioners for the post of HOUSE PHYSICIAN for 6 months.

Applications, with 2 recent testimonials, to the Hospital Secretary by 28th March, 1958.

ST. MATTHEW'S HOSPITAL, Shepherdess-walk, N.1. Applications are invited from registered medical practitioners for the post of SENIOR HOUSE OFFICER.

Apply to the Hospital Secretary, stating experience, and with copies of 2 recent testimonials, by 29th March, 1958.

ST. NICHOLAS HOSPITAL, Plumstead, S.E.18. Senior HOUSE OFFICER (Casualty Department). Recognised for F.R.C.S. There are 2 Senior House Officers in the Department, which provides good general experience. 6 months' resident appointment and may then be renewed.

Apply to Group Secretary, Memorial Hospital, Woolwich, S.E.18.

THE HOSPITAL FOR SICK CHILDREN, Great Ormond-street, London, W.C.1. There will be a vacancy for a HOUSE PHYSICIAN (Senior House Officer) on 15th June, 1958.

Further particulars and form of application, which must be returned not later than 8th April, 1958, may be obtained from the undersigned.

H. F. RUTHERFORD, House Governor and Secretary.

THE HOSPITAL FOR SICK CHILDREN, Great Ormond-street, London, W.C.1, and THE ROYAL FREE HOSPITAL, Gray's Inn-road, London, W.C.1. There will be a vacancy in June, 1958, for a SENIOR REGISTRAR in Radiology. The post is held jointly between the 2 Hospitals, the successful candidates being required to attend at The Hospital for Sick Children for 6 and at the Royal Free Hospital for 5 sessions per week.

Further particulars and forms of application, which must be returned not later than 8th April, 1958, may be obtained from the House Governor at the Hospital for Sick Children.

THE HOSPITAL FOR SICK CHILDREN, Great Ormond-street, London, W.C.1. There will be a vacancy on 8th June, 1958, for a RESIDENT DENTAL HOUSE SURGEON (Senior House Officer). The post is recognised for the Fellowship in Dental Surgery, Royal College of Surgeons. Experience is given in both oral surgery and orthodontics.

Further particulars and form of application, which must be returned not later than 8th April, 1958, are obtainable from the undersigned.

H. F. RUTHERFORD, House Governor and Secretary.

UNIVERSITY COLLEGE HOSPITAL, Gower-street, W.C.1. Applications are invited for the post of MEDICAL REGISTRAR for 1 year in the first instance from 1st June, 1958. This post will include a period of duty at the Whittington Hospital, N.19. Preference will be given to candidates holding higher qualifications.

Applications, with names of 2 referees, to T. F. W. MACKEOWN, Administrator and Secretary, by 28th March, 1958.

WANSTEAD HOSPITAL, Hermon Hill, E.11. (191 Beds.) Applications invited for post of SENIOR HOUSE OFFICER (resident), vacant 1st April. Salary £819 10s. less £150 p.a. for board-residence. Post includes care of general surgical and orthopædic cases and duties in Casualty Department. Post recognised for F.R.C.S. examination.

Applications, stating age, qualifications, experience, together with copies of 2 recent testimonials, should be sent to Secretary, Forest Group Hospital Management Committee, Langthorne-road, E.11.

WESTMINSTER HOSPITAL, St. John's-gardens, S.W.1. Applications invited for post of SURGICAL REGISTRAR for 1 year in first instance from 1st June, 1958.

Applications (5 copies), with names of 2 referees, to House Governor by 29th March.

WESTMINSTER HOSPITAL, St. John's-gardens, S.W.1. Applications invited for post of REGISTRAR in Anæsthetics for 1 year in first instance from 27th May, 1958.

Applications (9 copies), with names of 2 referees, to House Governor by 29th March.

WESTMINSTER HOSPITAL, St. John's-gardens, S.W.1. Applications invited for post of SENIOR HOUSE OFFICER in Anæsthetics for 1 year from 20th May, 1958.

Applications (9 copies), with names of 2 referees, to House Governor by 29th March.

WHIPPS CROSS HOSPITAL, Leytonstone, E.11. Appli-cations are invited from either fully or provisionally registered medical practitioners for 2 posts of HOUSE SURGEON in the Orthopædic Department. Both posts are recognised for the F.R.C.S.

Application forms from the Hospital Secretary, to be returned within 10 days of appearance of this advertisement.

WHITTINGTON HOSPITAL, London, N.19. Applications are invited for 1 post of HOUSE SURGEON (general surgery). Vacant 1st April, 1958. Post recognised for F.R.C.S. (Eng.). Pre-registration candidates may apply.

Application forms obtainable from Group Secretary, 46, Cholmeley-park, London, N.6 (ARChway 3070, extension 527), and returnable to the Medical Superintendent, Whittington Hospital, London, N.19, by 24th March, 1958.

WILLESDEN GENERAL HOSPITAL, Harlesden-road, London, N.W.10. Locum RESIDENT SURGICAL REGISTRAR required 1st April–6th May and 11th–19th June.

Apply Hospital Secretary.

ALTON, HAMPSHIRE. LORD MAYOR TRELOAR ORTHOPÆDIC HOSPITAL. Applications are invited from registered medical practitioners for the post of Whole-time ORTHOPÆDIC REGISTRAR. Post provides experience in non-pulmonary tuberculosis and general orthopædics and includes attendances at peripheral clinics. It is recognised for 6 months' training under F.R.C.S. regulations. The post is resident for married or single persons. Canvassing disqualifies, but visit to Hospital welcomed.

Write to the Secretary for application form.

ASHFORD HOSPITAL, Ashford, Middlesex. (500 Beds.) STAINES GROUP HOSPITAL MANAGEMENT COMMITTEE. Required, RESIDENT HOUSE SURGEONS (2) for Traumatic and Orthopædic Unit. 6-month appointments, suitable for pre-registration candidates.

Applications, stating age, qualifications and experience, with copies of up to 3 recent testimonials, to Medical Director of Hospital immediately.

BARROW-IN-FURNESS. NORTH LONSDALE HOSPI-TAL. Applications are invited for the resident post of HOUSE OFFICER (surgical) (recognised for pre-registration) at the North Lonsdale Hospital, Barrow-in-Furness. Post available immediately. Recognised for F.R.C.S.

Applications to the Group Secretary, Barrow and Furness Hospital Management Committee, 105, Abbey-road, Barrow-in-Furness.

BEBINGTON, CHESHIRE. CLATTERBRIDGE HOS-PITAL. CENTRAL WIRRAL GROUP.

HOUSE OFFICER (general medicine and geriatrics). Recognised pre-registration.

HOUSE OFFICER (general surgery). Recognised pre-registration.

Posts are tenable for 6 months from 1st March, 1958. Salary according to previous posts held.

Application forms, from Secretary, to be returned immediately.

BIRMINGHAM ACCIDENT HOSPITAL, Bath-row, Birm-INGHAM, 15. (215 Beds and 8 House Surgeons.) HOUSE SURGEON (resident). Hospital largest traumatic unit in the country and treats over 50,000 new patients each year. Recognised for purpose of casualty by R.C.S. (Eng.). Teaching programme by consultant staff. 6-month appointment, some of which may be spent in 42-bedded Medical Research Council's Burns Unit.

Apply, naming 2 referees, to Administrator.

BIRMINGHAM, 18. ALL SAINTS' HOSPITAL. Senior HOUSE OFFICER (resident) required (Male or Female). The Hospital is associated with Birmingham University for teaching of psychiatry. Training for Diploma in Psychological Medicine provided.

Applications, stating age and qualifications, to the Medical Superintendent.

BIRMINGHAM, 18. DUDLEY ROAD HOSPITAL. (780 Beds.) OBSTETRICS AND GYNÆCOLOGICAL DEPARTMENT. HOUSE SURGEON required. Vacant after 7th April, 1958. (Recognised for pre-registration and M.R.C.O.G.) The Department, under direction of a Senior Consultant Obstetrician, consists of 115 maternity beds, 100 neonatal cots and 60 gynæcological beds.

Detailed applications, with copies of 3 recent testimonials, to Group Secretary.

BIRMINGHAM. MOSELEY HALL HOSPITAL FOR CHILDREN, Alcester-road, BIRMINGHAM, 13. (65 Beds.) SENIOR HOUSE OFFICER (pædiatric). Now vacant. Resident/non-resident. Recognised for D.C.H.

Apply, with 3 testimonials, to Secretary, Birmingham (Selly Oak) Hospital Management Committee, Oak Tree-lane, Birmingham, 29.

BIRMINGHAM. RUBERY HILL HOSPITAL. (1020 Beds.) JUNIOR HOSPITAL MEDICAL OFFICER required, resident or non-resident, Male or Female. Valuable experience provided in the investigation, diagnosis and treatment of all forms of psychiatric illness. D.P.M. course, Birmingham University. Previous postgraduate psychiatric experience not essential. Ministry of Health terms and conditions of service.

Applications, stating name, age, nationality, qualifications, experience, and providing the names of 3 referees, to be sent as soon as possible, to the Group Secretary, Offices of the Hospital Management Committee, Rubery Hill Hospital, Birmingham.

BIRMINGHAM. THE UNITED BIRMINGHAM HOS-PITALS. THE CHILDREN'S HOSPITAL, Ladywood-road, BIRMINGHAM, 16. HOUSE OFFICER (medical) required for the Professorial Unit for 6 months from 7th April, 1958.

Forms of application may be obtained from the House Governor and should be returned not later than 31st March, 1958.

G. A. PHALP, Secretary to the Board of Governors.

BIRMINGHAM. THE UNITED BIRMINGHAM HOS-PITALS. Applications are invited for the appointment of RESIDENT CLINICAL PATHOLOGIST (Senior House Officer grade) at the Queen Elizabeth Hospital, Birmingham. There are 3 residents attached to the Department of Clinical Pathology. In addition to affording general experience in hæmatology, bacteriology, and some biochemistry, the appointment can provide opportunities for those studying for higher qualifications in medicine. The appointment is tenable for 1 year.

Application forms should be obtained from the Secretary to the Board of Governors, United Birmingham Hospitals, Queen Elizabeth Hospital, Birmingham, 15, and should be returned to him as soon as possible.

BIRMINGHAM. THE UNITED BIRMINGHAM HOS-PITALS. The following resident appointments are available for a period of 3 months commencing 7th April, 1958, and ending 6th July, 1958:

Queen Elizabeth Hospital

1 HOUSE SURGEON to the Surgical Professorial Unit.

1 HOUSE SURGEON to the Urological Department.

Forms of application may be obtained from the Secretary, The United Birmingham Hospitals, Queen Elizabeth Hospital, Birmingham, 15, and should be returned to him as soon as possible.

BIRMINGHAM, 9. LITTLE BROMWICH GENERAL HOSPITAL. PÆDIATRIC HOUSE PHYSICIAN (Male/Female). Vacant 1st May, 1958. Recognised for D.C.H. Includes duties on infectious diseases wards, Neonatal Department and clinics.

Applications to Physician-Superintendent, by 26th March, 1958.

BIRMINGHAM REGIONAL HOSPITAL BOARD.

(1) Coventry No. 20 Group, Coventry and Warwickshire Hospital, Coventry

REGISTRAR (orthopædic surgery). Hospital of St. Cross, Rugby. (156 Beds.) Some experience of traumatic surgery essential. Recognised F.R.C.S. Married accommodation available if required.

(2) Stoke-on-Trent Group, Princes-road, Stoke-on-Trent

(*a*) REGISTRAR (anæsthetics). Whole-time. North Staffordshire Royal Infirmary. (455 Beds.) Resident/non-resident. Possibility of housing accommodation. Higher qualification desirable. Recognised for D.A. and F.F.A. R.C.S. Medical Library available.

(*b*) REGISTRAR (thoracic surgery). Duties at Cheshire Joint Sanatorium (305 Beds) and North Staffordshire Royal Infirmary (475 Beds). Experience general surgery essential, higher qualification an advantage.

Application forms from Group Secretaries, to be returned by 24th March, 1958.

BISHOP AUCKLAND. THE GENERAL HOSPITAL. (350 Beds.) HOUSE SURGEON required. Recognised pre-registration appointment. Accommodation available for married officer with no children.

Apply, naming 2 referees, to Group Secretary, South West Durham Hospital Management Committee, at above address.

BISHOP'S STORTFORD, HERTFORDSHIRE. HERTS AND ESSEX GENERAL HOSPITAL. Applications invited for post of HOUSE OFFICER (surgical) (pre-registration). Salary £467 10s.–£522 10s. p.a. less £125 for residential emoluments. Appointment to commence 21st April, 1958.

Applications, stating age, nationality, qualifications and experience with copies of 2 recent testimonials or name of referees, to Hospital Secretary.

BLACKPOOL VICTORIA HOSPITAL (354 Beds.) ASSISTANT RESIDENT SURGICAL OFFICER (Senior House Officer grade). Vacant 1st June. Recognised for F.R.C.S. The post offers excellent experience in emergency and general surgery. The evening duties alternate with those of the Resident Surgical Officer.

Apply, stating age, qualifications and experience, together with the names and addresses of 2 referees, to the Group Secretary, Blackpool and Fylde Hospital Management Committee, Victoria Hospital, Blackpool.

BOLTON AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE.

Group Laboratories

RESIDENT PATHOLOGIST (Senior House Officer grade). Now vacant, tenable for 12 months and recognised for the Dip. Path.

Bolton District General Hospital (607 Beds)

RESIDENT HOUSE SURGEON. Now vacant, tenable for 6 months and recognised under pre-registration service scheme. Also recognised for F.R.C.S.

Applications, stating age, nationality, qualifications and experience, together with the names of 2 referees, to Group Secretary, The Royal Infirmary, Bolton.

BOURNEMOUTH. ROYAL VICTORIA HOSPITAL, Shelley-road, BOSCOMBE. BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of 2 GENERAL HOUSE SURGEONS. The appointments, which become vacant on the 24th March and mid-April, are recognised for the F.R.C.S. examination and for pre-registration purposes.

Applications to the Hospital Secretary.

BOURNEMOUTH. ROYAL VICTORIA HOSPITAL, Shelley-road, BOSCOMBE. (494 Beds.) BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of RESIDENT SENIOR HOUSE OFFICER in Pathology. The successful applicant will have opportunities for gaining experience in all 4 departments of the Laboratory, which is recognised for the Diploma in Pathology.

Applications to the Hospital Secretary.

BRIDGE OF EARN HOSPITAL, Perthshire. Applications are invited for the following posts :—

*HOUSE SURGEON, Fracture and Orthopædic Unit.
*HOUSE SURGEON, General Surgical Wards.
†HOUSE SURGEON or SENIOR HOUSE SURGEON, E.N.T. Ward.

Notes

Posts marked * are recognised by the Royal College of Surgeons under the regulations for the F.R.C.S.

Post marked † is recognised under the regulations for the D.L.O.

Applications, giving age, qualifications, experience and names of 2 referees, should be sent to the Group Medical Superintendent, Perth Royal Infirmary, Perth.

BRIGHTON. ROYAL SUSSEX COUNTY HOSPITAL. (314 Beds.) HOUSE SURGEON (pre-registration and recognised for F.R.C.S.), vacant mid-March.

Applications, stating usual particulars, and naming 2 referees, to the Administrative Officer, Royal Sussex County Hospital, Brighton, 7.

BRISTOL. COSSHAM AND FRENCHAY HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER (general surgery) required for duties at Frenchay Hospital and at Cossham Memorial Hospital. Resident appointment, unmarried accommodation only. Post vacant 25th May, 1958, tenable initially for 1 year. Recognised under Royal College of Surgeons fellowship regulations.

Applications, naming 2 referees, to the Group Secretary, Frenchay Hospital, Bristol, by 27th March, 1958.

BROMSGROVE, WORCESTERSHIRE. BARNSLEY HALL HOSPITAL. (For mental and nervous diseases—750 Beds.) Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER. Excellent opportunities for a young man to study in a modern mental hospital; modern treatments and up-to-date psychiatry. House available. Remuneration will be in accordance with the terms and conditions of service issued by the Ministry of Health.

Applications, stating age and experience, together with the names of 3 referees, to the Medical Superintendent.

BURTON-ON-TRENT GENERAL HOSPITAL. Locum SENIOR HOUSE OFFICER (medicine) required for a period of approximately 2 months, to mid-April, 1958.

Apply, Group Secretary.

BURY AND ROSSENDALE HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEONS (2). Applications are invited for 2 pre-registration posts in General Surgery which will be falling vacant during March, 1958. 1 of the posts is at Bury General Hospital and the other at Rossendale General Hospital.

Apply, stating age, qualifications and other details, to the Group Secretary at Bury General Hospital, Bury, Lancs.

CANTERBURY. KENT AND CANTERBURY HOSPITAL. (277 Beds.) The post of PÆDIATRIC HOUSE PHYSICIAN, recognised for D.C.H., includes work in the ward and Outpatient Department and also provides experience in the care of the newborn. Opportunities exist for the study of preventive medicine among children, and child guidance work. Post vacant early April, 1958. National Health Service salary and conditions.

Applications, together with copies of 2 testimonials, to be addressed to the Hospital Secretary at the above Hospital.

CANTERBURY. KENT AND CANTERBURY HOSPITAL. (277 Beds.) The post of SENIOR HOUSE PHYSICIAN is now vacant at Stodmarsh Road Annexe. Duties include care of 30-bedded unit of chest diseases, also work at the Chest Clinic and with the Pneumoconiosis Unit. National Health Service salary and conditions.

Applications, together with copies of 2 recent testimonials, to be addressed to the Hospital Secretary at the above Hospital.

CANTERBURY. KENT AND CANTERBURY HOSPITAL. (277 Beds.) The post of GENERAL SURGICAL AND UROLOGICAL HOUSE SURGEON (pre-registration or third post), which is recognised for the F.R.C.S., is now vacant. National Health Service salary and conditions.

Applications, together with copies of 2 recent testimonials, to be addressed to the Hospital Secretary at the above Hospital.

CANTERBURY. KENT AND CANTERBURY HOSPITAL. (277 Beds.) GYNÆCOLOGICAL HOUSE SURGEON required at Highland Court Annexe, a unit of 25 gynæcological beds situated 3 miles from the above Hospital, with all ancillary services available. Recognised for M.R.C.O.G. 6 months' appointment. Post vacant early April, 1958. National Health Service salary and conditions.

Applications, together with copies of 2 recent testimonials, to be addressed to the Hospital Secretary at the above Hospital.

CARDIFF. THE UNITED CARDIFF HOSPITALS. Applications are invited for the appointment of SENIOR HOUSE OFFICER in Ophthalmology at the Cardiff Royal Infirmary. Non-resident appointment, to commence 1st April.

Application forms are available from the Secretary to the Board at the Cardiff Royal Infirmary, Newport-road, Cardiff, and should be returned within 14 days of the appearance of this advertisement.

CARLISLE. CUMBERLAND INFIRMARY. 2 House SURGEONS required. Recognised for pre-registration purposes and for F.R.C.S. examination.

Reply immediately, with names for reference, to the Group Secretary, Cumberland Infirmary, Carlisle.

CARSHALTON, SURREY. QUEEN MARY'S HOSPITAL FOR CHILDREN. (A general children's hospital of 550 Beds.) RESIDENT MEDICAL REGISTRAR required to a firm comprising 180 Beds, including acute medical (60 Beds), poliomyelitis, rheumatism, and long-stay wards.

Applications, on forms obtainable from the Group Secretary, should be returned immediately.

CARSHALTON, SURREY. ST. HELIER HOSPITAL. (733 Beds.) PÆDIATRIC HOUSE OFFICER (not pre-registration.) Duties in 3 sick children's wards (mainly acute), Premature Baby Unit and Neonatal Department. Post recognised for D.C.H. Successful applicant will be required to start 18th April.

Apply immediately, giving age, qualifications and experience, with copies of recent testimonials and the names of referees, to the Secretary.

CHELTENHAM GENERAL HOSPITAL. (220 Beds.) HOUSE SURGEON required (pre- or post-registration) immediately. The post offers a wide experience in general surgery, gynæcology, and orthopædic surgery. Post recognised for the F.R.C.S.

Apply with names of 2 referees to Secretary, General Hospital, Cheltenham.

CHERTSEY, SURREY. ST. PETER'S HOSPITAL (late Botleys Park War Hospital). (430 Beds.) ORTHOPÆDIC HOUSE SURGEON (Senior House Officer or House Officer (intern) grade). 100 orthopædic beds. Post recognised for F.R.C.S. and pre-registration service. Salary in accordance with terms and conditions of National Health Service. Post vacant 21st April, 1958.

Applications, together with names and addresses of referees, to be sent to the Physician-Superintendent, St. Peter's Hospital, Chertsey, Surrey.

CHELMSFORD AND ESSEX HOSPITAL. (161 Beds.) Locum HOUSE SURGEON required. The post offers good surgical experience and is recognised for the F.R.C.S.

Applications to the Secretary, Chelmsford Hospital Management Committee, London-road, Chelmsford.

CHELMSFORD. ST. JOHN'S HOSPITAL. Applications are invited from registered practitioners for the post of RESIDENT PÆDIATRIC HOUSE OFFICER (Male or Female) commencing 31st March, 1958, to work in the Pædiatric Unit of the Chelmsford Hospital Group. The Unit includes a premature baby nursery of 10 Cots and a Neonatal Department in the maternity block of the Hospital. The Department is recognised for the D.C.H.

Applications, stating age, nationality, qualifications and experience, together with recent testimonials, should be received not later than 18th March, by the Group Secretary, Chelmsford Group Hospital Management Committee, Chelmsford and Essex Hospital, London-road, Chelmsford.

CATERHAM, SURREY. ST. LAWRENCE'S (Mental Deficiency) HOSPITAL. (2250 Beds.) JUNIOR HOSPITAL MEDICAL OFFICER required. Salary £852 10s.–£55–£1182 10s. Single residential accommodation available at a charge of £170 p.a.

Applications, giving full particulars and names of 2 referees, to Group Secretary, by 26th March, 1958.

COLCHESTER. ESSEX COUNTY HOSPITAL. (189 Beds.) Applications invited for post of SENIOR HOUSE OFFICER to Casualty and Radiotherapy Departments. Post tenable for 6 months or 1 year. Recognised for F.R.C.S.

Applications, with copies of 3 testimonials, to Group Secretary, Colchester Hospital Management Committee, 14, Pope's-lane, Colchester.

DENBIGH. THE NORTH WALES HOSPITAL FOR NERVOUS AND MENTAL DISORDERS. JUNIOR HOSPITAL MEDICAL OFFICER or SENIOR HOUSE OFFICER required. The Hospital has modern treatment facilities, and is recognised by the Conjoint Board for the purpose of their D.P.M. examination. House available for married man and family.

Applications, with names of 2 referees, to the Medical Superintendent.

DERBY. DERBYSHIRE ROYAL INFIRMARY. (396 Beds. Recognised for training for F.R.C.S.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT REGISTRAR (orthopædics) required. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 24th March, 1958, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

DERBY. DERBYSHIRE ROYAL INFIRMARY. (416 Beds.) SENIOR HOUSE OFFICER (casualty), vacant mid-April, resident post. Recognised for periods of 6 months' casualty training for F.R.C.S. The staffing of the department is a Senior Casualty Officer and 2 Senior House Officers.

Apply, stating age, experience, and 2 names for reference, to Secretary.

DERBY. DERBYSHIRE ROYAL INFIRMARY. (416 Beds.) SENIOR HOUSE OFFICER (E.N.T.), vacant immediately. Recognised for 6 months' training for F.R.C.S. (otolaryngology).

Apply, stating full details, with copies of 2 recent testimonials, to Secretary.

DERBY. DERBYSHIRE ROYAL INFIRMARY. Senior HOUSE OFFICER (ophthalmology). Vacant 31st March. Resident post. Recognised for F.R.C.S. (ophthalmology).

Apply immediately, stating full details and 2 names for reference, to Secretary.

DUDLEY, STOURBRIDGE AND DISTRICT HOSPITAL GROUP, BIRMINGHAM REGION.

The Corbett Hospital, Stourbridge (114 Beds)
HOUSE OFFICER (surgical), pre-registration. Post vacant now.

Wordsley Hospital, near Stourbridge (478 Beds)
HOUSE OFFICER (surgical), pre-registration. Post vacant now.

Apply Group Secretary, Guest Hospital, Dudley, Worcs.

DUNDEE (near). ASHLUDIE CHEST HOSPITAL, MONIFIETH, near DUNDEE, ANGUS. (222 Beds.) 1 HOUSE OFFICER (pre-registration) required for Surgical Wards immediately.

Applications, together with the names of 2 referees, to be submitted to the Physician-Superintendent as soon as possible.

EAST GRINSTEAD. QUEEN VICTORIA HOSPITAL. RESIDENT HOUSE OFFICER (Male or Female) required immediately for General Hospital. Appointment for 6 months in first instance; recognised for pre-registration purposes, and for F.R.C.S. examination.

Apply, stating age and experience, with names of 3 referees, to Hospital Secretary.

EDGWARE GENERAL HOSPITAL, Edgware, Middlesex. (647 Beds.) RESIDENT HOUSE SURGEON for above Hospital. Post vacant 31st March, 1958. 6 months' appointment. Recognised for F.R.C.S. and pre-registration purposes.

Applications, stating age, qualifications, experience and enclosing copies of up to 3 recent testimonials, to Medical Administrator of Hospital by 28th March, 1958.

EDGWARE GENERAL HOSPITAL, Edgware, Middlesex. (715 Beds.) NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. REGISTRAR in Pathology, resident or non-resident, required at above Hospital. Appointment for 1 year in first instance. Previous experience in pathology desirable. Hospital may be visited by appointment with the Medical Administrator.

Application forms obtainable from and returnable to Group Secretary, Hendon Group Hospital Management Committee, Edgware General Hospital, by 25th March, 1958.

EPPING. ST. MARGARET'S HOSPITAL. Applications are invited from fully registered medical practitioners for the posts of RESIDENT HOUSE PHYSICIANS (2) at the above Hospital as from 14th April, 1958. The appointments, which are in general medicine, are for 6 months, including duties at Honey Lane Hospital for part of this time.

Applications, with 2 recent testimonials, to reach the Group Secretary, Epping Group Hospital Management Committee, "Oak Cottage," The Plain, Epping, Essex, by 22nd March, 1958.

EPPING. ST. MARGARET'S HOSPITAL. Senior House OFFICER (anæsthetics) required, resident. Post vacant 28th March. Busy general Hospital, easy access to London. Good experience. Post recognised for D.A.

Applications, with copies of recent testimonials, to be sent to the Group Secretary, Epping Group Hospital Management Committee, Oak Cottage, The Plain, Epping, Essex, by 19th March, 1958.

ENFIELD, MIDDLESEX. CHASE FARM HOSPITAL. RESIDENT HOUSE SURGEON—third post. Vacant 30th March, 1958. Post provides experience and duties in general surgery and orthopædics. 6-month appointment. Post recognised for F.R.C.S.

Applications, with the names and addresses of 2 referees, to the Group Secretary, Enfield Group Hospital Management Committee, at Chase Farm Hospital.

ENFIELD. WAR MEMORIAL HOSPITAL, Chase Side, ENFIELD, MIDDLESEX. RESIDENT SENIOR HOUSE OFFICER required middle March, 1958, for General Medical and Surgical duties in acute General Hospital of 61 Beds. 12 months' appointment.

Applications, with names and addresses of 2 referees, to the Group Secretary, Enfield Group Hospital Management Committee, Chase Farm Hospital, The Ridgeway, Enfield, Middlesex.

EXETER. CITY HOSPITAL, Heavitree-road. Applications are invited from registered medical practitioners for the appointment of HOUSE PHYSICIAN to 2 active treatment wards of the area Geriatric Service based on the above Hospital. The appointment will include responsibility for 4 beds in the general medical wards.

Applications, with copies of 3 recent testimonials or naming 3 referees, to the Hospital Secretary.

EXETER. ROYAL DEVON AND EXETER HOSPITAL. Applications are invited from pre-registration and registered medical practitioners for the appointment of HOUSE SURGEON (obstetrics and gynæcology) at this Hospital. Vacant 3rd May, 1958.

Applications to the Hospital Secretary, with copies of 2 recent testimonials, by 22nd March, 1958.

EXMINSTER HOSPITAL, near Exeter. (1629 Beds, mental.) JUNIOR HOSPITAL MEDICAL OFFICER required immediately. Previous psychiatric experience advisable but not essential if candidate has good general experience. Accommodation available.

Applications, stating age, nationality, qualifications and experience, with the names of 2 referees, to The Group Secretary, Devon Mental Hospital Management Committee, Exminster Hospital, near Exeter, as soon as possible.

GODALMING, SURREY. MILFORD CHEST HOSPITAL. (314 Beds.) GODALMING, MILFORD AND LIPHOOK GROUP HOSPITAL MANAGEMENT COMMITTEE. Locum THORACIC REGISTRAR or SENIOR REGISTRAR required from 1st April, 1958. The Hospital deals with all forms of chest and cardiac diseases and has a busy thoracic surgical unit, experience in which would be an asset. Residential accommodation available for a single person.

Apply, giving experience, to the Physician-Superintendent.

GRAVESEND AND NORTH KENT HOSPITAL, Gravesend, Kent. MEDWAY AND GRAVESEND HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEON. Application are invited for this resident post (1 of 5 at the Hospital) which is approved for pre-registration purposes and recognised for the F.R.C.S. The successful applicant will be attached to 2 Consultant Surgeons with opportunities for extensive surgery and vascular work. Salary £467 10s. to £577 10s. p.a., according to experience.

Applications to Hospital Secretary stating age, experience, qualifications and nationality.

HALIFAX AREA HOSPITALS MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER in Obstetrics and Gynæcology required for duty at the Halifax General Hospital and Royal Halifax Infirmary. 100 obstetrical and 40 gynæcological beds. Post recognised for M.R.C.O.G. Vacant on 1st May, 1958.

Applications to be forwarded to the Secretary, Royal Halifax Infirmary, Halifax.

HALIFAX. ROYAL HALIFAX INFIRMARY. Senior HOUSE OFFICER in Anæsthetics required. Post recognised for F.F.A. R.C.S. and D.A.

Applications to be forwarded to the Secretary, Royal Halifax Infirmary, Halifax.

HASTINGS HOSPITAL MANAGEMENT COMMITTEE. Locum ORTHOPÆDIC REGISTRAR required for whole-time duties. Post vacant now. Remuneration £19 5s. per week. Non-resident.

Apply, giving details of qualifications and experience, to Group Secretary, 11, Holmesdale-gardens, Hastings.

HOVE GENERAL HOSPITAL. Senior House Officer (recognised for F.R.C.S.) required on 17th April, 1958. Duties of Resident Surgical Officer. Appointment for 1 year.

Applications, stating age, qualifications and full details of experience, together with names and addresses of 2 referees, to the Administrative Officer, Hove General Hospital, Hove, Sussex.

HOVE GENERAL HOSPITAL. Pre-registration House SURGEON (with ward and casualty duties) required immediately for a period of 6 months. This post is recognised for the F.R.C.S. and provides a wide experience in an active surgical unit.

Applications, stating age, qualifications, and full details of experience, together with the names and addresses of 2 referees, to the Administrative Officer, Hove General Hospital, Hove, Sussex.

HEMEL HEMPSTEAD, HERTFORDSHIRE. ST. PAUL'S AND WEST HERTS HOSPITALS. HOUSE PHYSICIAN (pre-registration) required to commence 18th April, 1958.

Applications, giving details and enclosing copies of 2 recent testimonials, should be sent to the Secretary, St. Paul's Hospital, Hemel Hempstead, Herts, by 22nd March.

HEMEL HEMPSTEAD, HERTFORDSHIRE. WEST HERTS HOSPITAL. Applications are invited for the post of SENIOR HOUSE OFFICER (pædiatrics), which is recognised for the D.C.H.

Applications, together with copies of 2 recent testimonials, should be sent to the Hospital Secretary at once.

HEMEL HEMPSTEAD, HERTFORDSHIRE. WEST HERTS HOSPITAL. Locum Tenens CASUALTY OFFICER (Junior Hospital Medical Officer) required for period 15th April-5th May (inclusive).

Please apply to the Hospital Secretary.

HOLT, NORFOLK. KELLING HOSPITAL AND DEPARTMENT OF THORACIC SURGERY. Applications are invited for the appointment of RESIDENT SENIOR HOUSE OFFICER which will become vacant on 1st April, 1958. This Hospital (180 Beds) deals with tuberculous and non-tuberculous chest conditions and offers excellent experience in chest medicine and thoracic surgery. Married accommodation available.

Applications, stating age, sex, qualifications, nationality and experience, together with names of 2 referees, to the Group Secretary, Cromer Area Hospital Management Committee, Cliff-avenue, Cromer, Norfolk, who will be pleased to supply any other information concerning the appointment.

HUDDERSFIELD ROYAL INFIRMARY. (285 Beds.) HUDDERSFIELD HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEON required to commence duty immediately. The post is recognised as a pre-registration appointment and for the F.R.C.S. Salary in accordance with national scale.

Applications, together with copies of 3 recent testimonials, to be addressed to the undersigned as soon as possible.

H. J. JOHNSON,
Secretary to the Management Committee.

The Royal Infirmary, Huddersfield.

HUDDERSFIELD. ST. LUKE'S HOSPITAL. (235 Beds.) HUDDERSFIELD HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of RESIDENT MEDICAL OFFICER (Senior House Officer grade) at the above Hospital, to commence duties on 1st April, 1958. The duties will be mainly surgical, in a hospital which caters for chronic sick, children, maternity and acute medical and surgical patients. Salary in accordance with the terms and conditions of service for hospital medical and dental staff, £819 10s. p.a.

Applications, together with copies of 3 recent testimonials, to be sent to the undersigned as soon as possible.

H. J. JOHNSON,
Secretary to the Management Committee.

The Royal Infirmary, Huddersfield.

ILFORD, ESSEX. GOODMAYES HOSPITAL. Senior HOUSE OFFICER required from 1st May, 1958, for mental hospital situated within easy reach of the centre of London. All forms of modern psychiatric treatment available. Facilities given to study for higher qualifications. Salary £819 10s. p.a., less £150 for residential amenities if resident.

Applications, stating age, experience and qualifications, to Physician-Superintendent together with 2 copies of recent testimonials, as soon as possible.

IPSWICH AND EAST SUFFOLK HOSPITAL (Anglesea-ROAD WING). (350 Beds.) Applications are invited for the post of HOUSE SURGEON to the Fracture and Orthopædic Department. Approved pre-registration post.

Applications, with copies of recent testimonials, to the Hospital Secretary.

IPSWICH AND EAST SUFFOLK HOSPITAL (Anglesea-ROAD WING). (350 Beds.) Applications invited for post of HOUSE SURGEON to 2 Consultant General Surgeons. Post recognised for pre-registration and F.R.C.S. examination.

Applications, with copies of recent testimonials, to Hospital Secretary.

IPSWICH AND EAST SUFFOLK HOSPITAL (Heath-ROAD WING), IPSWICH. Pre-registration post of HOUSE SURGEON to General Surgeon vacant. Recognised for R.C.S. examination.

Applications, with copies of recent testimonials, to Hospital Secretary.

KENDAL. WESTMORLAND COUNTY HOSPITAL. (82 Beds.) RESIDENT SENIOR HOUSE OFFICER (medical). Duties include the care of acute cases under the supervision of Consultant Physicians, and attendance at consultative clinics. Post tenable for 1 year.

Applications, with full particulars and names of 2 referees, to be addressed to Group Secretary, Royal Lancaster Infirmary, Lancaster.

KIDDERMINSTER AND DISTRICT GENERAL HOSPITAL, WORCESTERSHIRE. (112 Beds.) Applications are invited for the pre-registration post of HOUSE SURGEON at the above Hospital.

Applications, with the names of 3 referees, to the Hospital Secretary.

KING'S LYNN. WEST NORFOLK AND KING'S LYNN GENERAL HOSPITAL. (146 Beds.) KING'S LYNN AREA HOSPITALS MANAGEMENT COMMITTEE. Applications are invited from medical practitioners, qualified or pre-registration, for the post of RESIDENT HOUSE SURGEON (obstetrics/gynæcology) at the above Hospital. Appointment will be for 6 months in the first instance. Post vacant early April. 9 residents employed.

Applications, with names and addresses of 2 referees, to be forwarded to the Group Secretary of the above Committee, St. James' Hospital, King's Lynn, Norfolk.

KINGSTON HOSPITAL, Wolverton-avenue, Kingston-on-THAMES. KINGSTON GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from suitably qualified Medical Officers for the post of SENIOR HOUSE OFFICER (gynæcology). The post, which will be vacant on 1st June, 1958, is recognised for M.R.C.O.G. purposes.

Applications, stating age, qualifications and experience, together with 2 recent testimonials, should be sent to the Physician-Superintendent of the Hospital.

KETTERING AND DISTRICT GENERAL HOSPITAL, NORTHAMPTONSHIRE. Applications are invited for the post of HOUSE SURGEON (pre-registration). Post recognised for F.R.C.S.

Applications, stating age, experience, and qualifications, together with copies of 3 recent testimonials, to be sent to the Group Secretary at the above address.

LEAMINGTON SPA. WARNEFORD GENERAL HOSPITAL. (197 Beds.) CASUALTY OFFICER (Senior House Officer), Male or Female, resident or non-resident, and suitable for one reading for higher qualifications, being recognised for F.R.C.S., affording contact with all specialist units in the Hospital.

Applications, with names and addresses of 3 referees, to Hospital Secretary.

LEEDS REGIONAL HOSPITAL BOARD. Registrar vacancies.

Anæsthetics

Hull A, B, and East Riding Groups. Recognised for the F.F.A. R.C.S. Duties may include thoracic anæsthesia. Non-resident.

Chest Diseases

Castle Hill Sanatorium, Cottingham, East Yorkshire. (220 Beds.) Resident.

General Surgery

St. Luke's Hospital, Bradford (160 general surgical beds.) Recognised for F.R.C.S. Preferably resident. Only single accommodation available at the present time.

Applications, stating age, qualifications and details of present and previous appointments with dates, together with the names and addresses of 3 referees to the Secretary, Joint Registrars Committee, Park-parade, Harrogate, by 1st April, 1958.

LEEDS. THE UNITED LEEDS HOSPITALS. THE GENERAL INFIRMARY AT LEEDS. REGISTRAR in Thoracic Surgery required from 1st April, 1958, for 1 year in the first instance. Work will include a considerable amount of cardiac and upper abdominal surgery.

Applications, stating age, experience, qualifications, previous posts, with dates, and 3 names for reference, to be sent to the Sub-Dean, School of Medicine, Leeds, 2, as soon as possible.

LEEDS. UNIVERSITY OF LEEDS. UNITED LEEDS HOSPITALS. Applications are invited for the post of SENIOR REGISTRAR AND TUTOR in Psychiatry. The successful candidate will be a member of the University Department of Psychiatry and the duties will include work at the General Infirmary at Leeds with which the University Department is associated and such other duties as may be assigned to him by the Head of the University Department.

Applications (3 copies), stating date of birth, qualifications and details of present and previous appointments with dates, and experience of teaching, together with the names of 3 referees, should reach the Registrar, The University, Leeds, 2 (from whom further particulars may be obtained), not later than 14th April, 1958.

LEEK (near). ST. EDWARD'S HOSPITAL, Cheddleton, near LEEK, STAFFORDSHIRE. JUNIOR HOSPITAL MEDICAL OFFICER, previous Mental Hospital experience not essential. This Hospital offers opportunities for gaining experience in all branches of psychiatry. Terms and conditions of service will be as approved for hospital medical staff employed in the National Health Service. Salary £852–£55–£1182. Single furnished quarters, or unfurnished house on Hospital estate available for a married man.

Applications as soon as possible to the Medical Superintendent.

LEICESTER ROYAL INFIRMARY. Applications are invited for the resident posts of HOUSE SURGEON (3) available for pre-registration candidates, vacant 1st April. Recognised for the F.R.C.S.

Applications, stating age, and qualifications, together with copies of recent testimonials, to the Group Secretary, The Leicester No. 1 Hospital Management Committee, The Leicester Royal Infirmary, forthwith.

LOUTH. COUNTY HOSPITAL. (215 Beds. Recognised for training for F.R.C.S.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT or NON-RESIDENT SURGICAL REGISTRAR required 1st April. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 24th March, 1958, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

LIVERPOOL. THE UNITED LIVERPOOL HOSPITALS. Applications are invited for temporary appointment to the post of REGISTRAR in Radiology for the period to 30th September, 1958. The person appointed will be eligible to apply during the summer for appointment for the year beginning 1st October, 1958.

Apply by 29th March, 1958, on form obtainable from the Secretary, 80, Rodney-street, Liverpool, 1.

LIVERPOOL. THE UNITED LIVERPOOL HOSPITALS. Applications are invited for temporary appointment to the post of SENIOR REGISTRAR in Otorhinolaryngology for the period to 30th September, 1958, for duty at Liverpool Ear, Nose and Throat Infirmary. The person appointed will be eligible to apply in the summer of 1958 for appointment for the year beginning 1st October, 1958.

Apply by 26th March, 1958, on form obtainable from the Secretary, 80, Rodney-street, Liverpool, 1.

LIVERPOOL. THE UNITED LIVERPOOL HOSPITALS. Applications are invited for the following House Officer post which has not yet been filled for the period to 31st August, 1958:—

Stanley Hospital

CASUALTY OFFICER AND ORTHOPÆDIC HOUSE SURGEON (combined post).

The post is open to registered and pre-registration applicants.

Apply immediately on form obtainable from the Secretary, 80, Rodney-street, Liverpool, 1.

LIVERPOOL. THE UNITED LIVERPOOL HOSPITALS. Applications are invited for temporary appointment as SENIOR HOUSE OFFICER in Ophthalmology at St. Paul's Eye Hospital for the period to 30th September, 1958.

Apply immediately on form obtainable from the Secretary, 80, Rodney-street, Liverpool, 1.

LIVERPOOL. THE UNITED LIVERPOOL HOSPITALS, ST. PAUL'S EYE HOSPITAL. Applications are invited for appointment as Locum REGISTRAR in Ophthalmology for the period 1st April to 31st May, 1958.

Apply immediately, with full details of qualifications, previous posts, &c., and the names and addresses of 2 referees, to the Secretary, The United Liverpool Hospitals, 80, Rodney-street, Liverpool, 1.

MAIDENHEAD HOSPITAL, Berkshire. Applications invited for post of HOUSE PHYSICIAN, vacant 19th April. Pre-registration post.

Applications, stating age, qualifications and nationality, with names of 3 referees, to Secretary.

MAIDSTONE. WEST KENT GENERAL HOSPITAL. (141 Beds.) MID-KENT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the pre-registration post of HOUSE SURGEON. 6 months' appointment. Vacant now. Recognised for F.R.C.S. Salary at the rate of £467 10s.–£577 10s. p.a. A deduction at the rate of £125 a year is made for board and lodging, and other services provided.

Applications should be forwarded, as soon as possible, to the Administrative Officer at the Hospital.

MANCHESTER, 20. CHRISTIE HOSPITAL AND HOLT RADIUM INSTITUTE. SOUTH MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the post of RESIDENT SENIOR HOUSE OFFICER (radiotherapy) at the above Hospital. Suitable applicants will be eligible for the D.M.R.T. course commencing in April, 1958.

Applications, with full details and the names of 2 referees, to the Group Secretary, Withington Hospital, Manchester, 20, immediately.

MANCHESTER. MONSALL HOSPITAL. Registrar for the Chest Unit at above Hospital. The Unit comprises 96 tuberculous and 48 non-tuberculous beds and offers excellent experience in thoracic medicine and surgery. The appointment also includes duties at the outpatients' clinic held at the Northern Hospital, Manchester.

Applications, stating age, present post, experience and names of 2 referees, to be forwarded immediately to The Secretary, Monsall Hospital, Newton Heath, Manchester, 10.

MANCHESTER REGIONAL HOSPITAL BOARD. Regis-TRAR for the Geriatric Department of the Bolton and District Group of hospitals. Vacant mid-March.

Applications, stating age, nationality, qualifications, experience, and the names of 2 referees, should be sent immediately to Group Secretary, Bolton and District Hospital Management Committee, The Royal Infirmary, Bolton.

MANCHESTER REGIONAL HOSPITAL BOARD. South MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the post of REGISTRAR in Radiotherapy at the Christie Hospital and Holt Radium Institute, Manchester. Candidates must hold either the Diploma in Radiotherapy or an F.R.C.S. or M.R.C.P.

Applications, with full details, to be forwarded to the Group Secretary, Withington Hospital, Manchester, immediately.

MANCHESTER. UNITED MANCHESTER HOSPITALS. ROYAL EYE HOSPITAL, MANCHESTER, 13. SENIOR REGISTRAR in Ophthalmology. Whole-time, non-resident post, tenable for 12 months, renewable. Previous experience essential.

Application form obtainable from the Secretary to the Board of Governors, United Manchester Hospitals, Manchester Royal Infirmary, Manchester, 13, to be returned as soon as possible.

MARKET DRAYTON, SHROPSHIRE. CHESHIRE JOINT SANATORIUM. SENIOR HOUSE OFFICER required for inpatient and outpatient duties with Thoracic Surgical Unit dealing with tuberculous and non-tuberculous cases for a population of approximately 500,000.

Applications to Medical Superintendent at the Sanatorium.

MERTHYR TYDFIL. ST. TYDFIL'S HOSPITAL. (375 Beds.) JUNIOR HOSPITAL MEDICAL OFFICER (casualty–resident). New modern Casualty Department. The appointment is subject to a limited tenure of 3 years. Salary £852 10s.–£55–£1182 10s. p.a., less £170 for residence.

Apply, with full particulars and copies of 2 recent testimonials, to the Group Secretary, Merthyr and Aberdare Hospital Management Committee, St. Tydfil's Hospital, Merthyr Tydfil.

MIDDLESBROUGH. POOLE HOSPITAL, Nunthorpe, MIDDLESBROUGH. (Tuberculosis—308 Beds.) Applications are invited for the appointment of RESIDENT SENIOR HOUSE OFFICER (married accommodation available) for general duties on medical and surgical wards (adults and children). Salary and conditions of service in accordance with the Ministry of Health regulations. This Hospital is a most modern one with an active thoracic surgery unit.

Applications, stating age, qualifications and previous experience, together with the names of 3 referees, to be sent immediately to the Group Secretary, Cleveland Hospital Management Committee, West Lane Hospital, Middlesbrough.

MITCHAM. WILSON HOSPITAL, Cranmer-road, MITCHAM, SURREY. SENIOR HOUSE OFFICER (surgical). Duties mainly in Casualty Department. Post vacant 1st May.

Applications, enclosing copies of recent testimonials and the names of 2 referees, to the Group Secretary, St. Helier Hospital, Carshalton, Surrey.

NEWCASTLE GENERAL HOSPITAL. Senior House OFFICERS (2), general surgery. These are resident posts, vacant in March, 1958.

Applications, together with names and addresses of 2 referees, should be sent to the Secretary, Newcastle General Hospital, Newcastle upon Tyne, 4.

NEWCASTLE REGIONAL HOSPITAL BOARD. Regis-TRAR SURGEON, whole-time, South Shields Group of hospitals—main hospital, Ingham Infirmary (165 Beds). Post recognised for F.R.C.S. Single accommodation available.

Applications, with names and addresses of 3 referees, to Senior Administrative Medical Officer, Regional Hospital Board, Benfield-road, Newcastle upon Tyne, 6, within 14 days.

NEATH GENERAL HOSPITAL, Neath, Mid Glamorgan HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER (paediatrics). This Hospital is recognised for the Diploma in Child Health. Salary at the rate of £819 10s. p.a. less a deduction of £150 p.a. in respect of residential emoluments.

Applications, naming 2 referees, to be addressed to the Group Secretary, Mid Glamorgan Hospital Management Committee, 8, Wind-street, Neath.

NEWMARKET GENERAL HOSPITAL, Suffolk. Applica-tions are invited for the post of HOUSE SURGEON, vacant now. Duties include house charge of general surgical and some eye cases. Post resident and available for 6 months; recognised for pre-registration.

Applications, with copies of 3 testimonials, to Medical Superintendent.

NEWTON ABBOT HOSPITAL. (General section, 65 Beds.) RESIDENT SENIOR HOUSE SURGEON, Male or Female, required approximately end May, 1958. Married quarters available.

Applications, quoting Ref. F.364/40, stating qualifications, nationality, age, with copy testimonials, to be sent to the Group Secretary, Torquay District Hospital Management Committee, Torbay Hospital, Torquay, South Devon.

NEWTON ABBOT HOSPITAL, South Devon. Senior HOUSE OFFICER (medicine), Male or Female, required 24th March, 1958. Duties divided equally between 20 acute medical beds in general section and 140 geriatric beds. This officer is also required to stand in when Senior House Surgeon otherwise engaged. Married quarters available.

Applications, stating qualifications, nationality, age, with copy testimonials, to be sent to the Group Secretary, Torquay District Hospital Management Committee, Torbay Hospital, Torquay, S. Devon.

NOTTINGHAM CITY HOSPITAL AND SKIN CLINIC. SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time NON-RESIDENT REGISTRAR (Dermatology) required. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 24th March, 1958, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

NOTTINGHAM EYE HOSPITAL. Senior House Officer required, duties to commence mid-April, 1958. Salary and conditions of service in accordance with Ministry regulations.

Applications, stating age, qualifications and experience, together with copies of testimonials, to be sent to the Group Secretary, General Hospital, Nottingham.

NOTTINGHAM GENERAL HOSPITAL. Senior House OFFICER (anæsthetics) required as soon as possible. The post is recognised for the D.A. and the F.F.A. R.C.S. This is a busy general hospital giving experience in all branches of surgery.

Applications, stating age, nationality, qualifications and experience, together with copies of testimonials, to be sent to the Group Secretary.

NOTTINGHAM. THE HOGARTH RADIOTHERA-PEUTIC CENTRE, GENERAL HOSPITAL, NOTTINGHAM. SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT OR NON-RESIDENT SENIOR HOUSE OFFICER or REGISTRAR in Radiotherapy required. (Possession of a higher qualification in medicine or surgery or the D.M.R. (T) part 1 would qualify for appointment of Registrar.) Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 24th March, 1958, giving age, nationality, qualifications, present and previous appointments, with dates, naming 3 referees.

OXFORD REGIONAL HOSPITAL BOARD. Registrar in General Surgery to Kettering and District General Hospital. (60 surgical beds.) A wide range of experience in general surgery available. Single or married accommodation available. Appointment for 1 year only from 1st April, 1958.

Applications, on forms obtainable from the Secretary, Registrars Committee, 43, Banbury-road, Oxford, by 27th March.

OXFORD REGIONAL HOSPITAL BOARD. Locum SENIOR REGISTRAR in General Medicine at Northampton General Hospital. Whole-time, for 1 year from 1st April, 1958. Good opportunity for wide experience.

Applications, with full details of experience and names of 2 referees, to Secretary, Regional Hospital Board, 43, Banbury-road, Oxford, as soon as possible.

OXFORD REGIONAL HOSPITAL BOARD. Registrar in Obstetrics and Gynæcology to the General Hospital, Northampton (62 obstetric beds, 38 gynæcology beds). Recognised for the M.R.C.O.G.

Applications on forms obtainable from the Secretary, Registrars Committee, 43, Banbury-road, Oxford, should reach him by 24th March.

OXFORD REGIONAL HOSPITAL BOARD. Resident REGISTRAR to the Plastic Surgery and Jaw Injuries Centre, and the Burns Unit, Stoke Mandeville Hospital, Aylesbury. The appointment will be for 1 year in the first instance and eligible for extension to a second year.

Applications, on forms obtainable from the Secretary, Registrars Committee, 43, Banbury-road, Oxford, should reach him by 24th March.

PAISLEY. ROYAL ALEXANDRA INFIRMARY. Junior HOSPITAL MEDICAL OFFICER for general duties required immediately.

Applications to Group Medical Superintendent, Royal Alexandra Infirmary, Paisley.

PETERBOROUGH. THE MEMORIAL HOSPITAL AND OBSTETRIC ANNEXES. PETERBOROUGH AND STAMFORD HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEON (obstetrics and gynæcology). Applications are invited for vacancy on 14th April, 1958. Busy Gynæcological Department and 54 obstetric beds. Unit consists of a Consultant, Registrar and 2 House Surgeons. Recognised for D.Obst.R.C.O.G.

Application forms from Secretary.

PLYMOUTH. SOUTH DEVON AND EAST CORN-WALL HOSPITAL, FREEDOM FIELDS. Central Casualty Department. RESIDENT SENIOR HOUSE OFFICER in Casualty vacancies, 1 immediately, and 1st April, 1958. Recognised for the F.R.C.S.

Applications, stating names of 3 referees, to be sent to the Group Secretary.

PORTSMOUTH GROUP HOSPITAL MANAGEMENT COMMITTEE.

(1) **Saint Mary's Hospital**

HOUSE SURGEON (pre-registration). Vacant now (2 posts).

(2) **Royal Portsmouth Hospital**

(*a*) HOUSE SURGEON (pre-registration). Vacant now.

(*b*) SENIOR HOUSE OFFICER required in Orthopædic Department (104 Beds). Vacant 1st April, 1958.

Applications, stating age, experience and qualifications, together with the names of 2 referees, should be forwarded as soon as possible to E. H. HURST.

St. Mary's Hospital, Milton-road, Portsmouth.

READING. BATTLE HOSPITAL. (391 Beds.) Reading AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the post of RESIDENT JUNIOR HOUSE SURGEON (pre- or post-registration) required in the Accident and Orthopædic Department. F.R.C.S. recognised. Also casualty duties.

Apply, stating age, qualifications with dates, nationality, present post, with copy of recent testimonial, to Secretary.

READING COMBINED HOSPITALS. Area Department OF OBSTETRICS AND GYNÆCOLOGY. (100 Beds.) Applications are invited from registered medical practitioners, Male and Female, for the resident post of GYNÆCOLOGICAL HOUSE SURGEON at the Royal Berkshire Hospital, Reading. Vacant 8th April, 1958, and tenable for 6 months. Post recognised for M.R.C.O.G.

Write, stating age, qualifications with dates, nationality and present post, with copy of 1 recent testimonial, to Secretary.

READING. ROYAL BERKSHIRE HOSPITAL. Applications are invited from registered medical practitioners for the post of RESIDENT ASSISTANT PATHOLOGIST (1 of 2), vacant on 15th April, 1958, and tenable for 6 months. Salary £577 10s. p.a.

Write, stating age, qualifications with dates, nationality and present post, with copies of 2 recent testimonials, to Secretary.

RHYL. ROYAL ALEXANDRA HOSPITAL. (138 Beds.) Applications are invited from registered medical practitioners for the post of HOUSE PHYSICIAN for the Departments of Medicine and Pædiatrics at the above Hospital. Post vacant 1st April, 1958.

Applications, stating age and experience, with copies of 2 testimonials, to be sent to the Group Secretary, Clwyd and Deeside Hospital Management Committee, "Rhianfa," Russell-road, Rhyl.

ROMFORD, ESSEX. VICTORIA HOSPITAL. (99 Beds.) RESIDENT HOUSE SURGEON (Male) required immediately. Not pre-registration appointment.

Applications should be forwarded to the Secretary, Romford Group Hospital Management Committee, Oldchurch Hospital, Romford.

ROMFORD, ESSEX. VICTORIA HOSPITAL. (99 Beds.) RESIDENT HOUSE PHYSICIAN (Male) required from 21st April, 1958. Not pre-registration appointment.

Applications should be forwarded to the Secretary, Romford Group Hospital Management Committee, Oldchurch Hospital, Romford.

SCOTLAND. NORTHERN REGIONAL HOSPITAL BOARD invite applications for a Post under the Combined Training Scheme in Hospital and General Practice in which the Board and the Executive Council for the County of Inverness are associated. The Scheme provides a training of 2 years' duration for young medical practitioners intending to enter general medical practice or a specialty. Concurrent experience is given in various departments of the hospitals and with selected general practitioners in the town of Inverness. The trainees' time is divided equally between hospital work and general practice. The post is non-resident. It is graded at Senior House Officer or Registrar level according to the hospital duties and the corresponding salaries are : £819 10s. rising in the second year to £850, and £850 rising in the second year to £935.

Candidates should apply by 5th April, 1958, on forms obtainable from the undersigned, by whom further particulars will be supplied on request. A. M. FRASER, M.D.,

Secretary and Administrative Medical Officer.

Office of the Northern Regional Hospital Board,
17, Old Edinburgh-road, Inverness.

SCOTLAND. WESTERN REGIONAL HOSPITAL BOARD. Applications are invited for the following appointments, which will be for 1 year in the first instance :—

SENIOR REGISTRAR in Dermatology based at Stobhill General Hospital, Glasgow.

REGISTRAR in Dentistry for duties in the Oral Surgery Department, Glasgow Dental Hospital.

REGISTRAR in Plastic Surgery at the Royal and Western Infirmaries, Glasgow, for duties with the Regional Consultant in Plastic Surgery.

REGISTRAR in Psychiatry for duties at Bellsdyke Mental Hospital, Larbert, and at H.M. Institution, Polmont.

Applications (12 copies), stating date of birth, qualifications, experience, present appointment, and the names of 3 referees, to reach the Secretary, Western Regional Hospital Board, 64, West Regent-street, Glasgow, C.2, by 29th March, 1958.

SHEFFIELD, 6. KING EDWARD VII ORTHOPÆDIC HOSPITAL. SHEFFIELD NO. 3 HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of a SENIOR HOUSE OFFICER. The Hospital has 154 Beds, 100 of which are occupied by children. It is a modern unit for the treatment of poliomyelitis and has close contact with a nearby infectious diseases hospital. The post would suit applicants interested in children's diseases, and there is a fair amount of general medical work.

Applications, with names of 2 referees, to the Group Secretary, Sheffield No. 3 Hospital Management Committee, Lodge Moor Hospital, Sheffield, 10.

SHEFFIELD, 10. LODGE MOOR HOSPITAL. (467 Beds.) SHEFFIELD NO. 3 HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the post of RESIDENT SENIOR HOUSE OFFICER in Infectious Diseases commencing early April, 1958. Candidates should have held a resident appointment in a hospital. Salary £819 10s. p.a., subject to a deduction of £150 p.a. for residential emoluments. The appointment is normally for 1 year, subject to 1 month's notice on either side.

Applications, stating age, qualifications, &c., to the Group Secretary, Sheffield No. 3 Hospital Management Committee, Lodge Moor Hospital, Sheffield, 10.

SHEFFIELD REGIONAL HOSPITAL BOARD. Sheffield NO. 4 HOSPITAL MANAGEMENT COMMITTEE. Radiotherapy Centres. Medical Men and Women desirous of taking up radiotherapy are invited to apply for the post of RADIOLOGICAL OFFICER at Sheffield. The appointment will have the status of a Senior House Officer on a salary of £819 10s. p.a. Approved courses for the D.M.R.T. (R.C.P. and S.) are held at the Sheffield National Centre for Radiotherapy, and will be open to the successful candidate, facilities being given to attend these.

Applications for further particulars should be addressed to the Secretary, Broom Cross, Tree Root-walk, Sheffield, 10.

SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time NON-RESIDENT SENIOR REGISTRAR (psychiatry) required for duties at the Towers Hospital, Leicester, and Children's Psychiatric Clinics in Leicester and Leicestershire. Possession of a higher qualification desirable. Appointment for 1 year in first instance reviewable annually.

Application form and further details from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield. Forms to be returned by 31st March, 1958.

SHEFFIELD. THE UNITED SHEFFIELD HOSPITALS BOARD OF GOVERNORS and SHEFFIELD REGIONAL HOSPITAL BOARD. Reciprocal Training Scheme for Senior Registrars. Whole-time SENIOR REGISTRAR in E.N.T. Surgery required with initial tenure of appointment at the Royal Hospital, Sheffield. Appointment for 1 year in the first instance and renewable annually thereafter. Successful candidate will be transferred to the Royal Infirmary, Leicester, for the second phase of the appointment, in accordance with the arrangements under the Reciprocal Training Scheme. Renewal of appointment and transfer will be subject to satisfactory work and progress.

Applications, with the names of 3 referees, to the Chief Administrative Officer, The United Sheffield Hospitals, West-street, Sheffield, 1, not later than 29th March. 1958.

SHEFFIELD. THE UNITED SHEFFIELD HOSPITALS. Applications invited for the following posts :—

(*a*) ANÆSTHETIC REGISTRAR. Post vacant 13th May, 1958. Successful candidate will be required to work in any of the units of the United Sheffield Hospitals.

(*b*) RESIDENT SURGICAL OFFICER (Registrar grade) at the Royal Hospital. Vacant 31st May, 1958. Post is ideal for candidates working for final F.R.C.S. The holder acts as Registrar to a General Surgical Unit.

(*c*) RESIDENT SENIOR HOUSE OFFICER in Clinical Pathology at the Royal Hospital. Pathological experience not essential, but candidates must have previous clinical experience. The successful candidate will work in turn in the different branches of clinical pathology in the laboratories of the United Sheffield Hospitals.

(*d*) Registered medical practitioners are invited to apply for the resident post of HOUSE PHYSICIAN to the Professorial Unit at the Children's Hospital. Vacant 1st May, 1958 (6 months).

Applications for the above posts should state age, qualifications and experience, with the names of 3 referees, and should be sent as follows :—

For posts (*a*) and (*b*) : Chief Administrative Officer, The United Sheffield Hospitals, West-street, Sheffield, 1, not later than 22nd March.

For post (*c*) to the Superintendent, Royal Hospital, West-street, Sheffield, 1, at once.

For post (*d*) to the Superintendent, Children's Hospital, Western-bank, Sheffield, 10, not later than 24th March, 1958.

Copy testimonials may be sent with applications for posts (*c*) and (*d*).

SHREWSBURY. CROSS HOUSES HOSPITAL. Obstetric HOUSE SURGEON. Pre-registration post. Vacant 1st April, 1958.

Applications, with copy testimonials, to Group Secretary, Shrewsbury Hospital Group, Royal Salop Infirmary, Shrewsbury.

SHREWSBURY. ROYAL SALOP INFIRMARY/COP-THORNE HOSPITAL. (500 Beds.) HOUSE PHYSICIAN, pre-registration candidates eligible. Vacant 23rd April, 1958.

Applications, with copy testimonials, to Group Secretary, Shrewsbury Hospital Group, Royal Salop Infirmary, Shrewsbury.

SOUTHAMPTON. ROYAL SOUTH HANTS HOS-PITAL. (374 Beds.) RESIDENT HOUSE SURGEONS (2) required immediately. Pre-registration candidates eligible. The posts are recognised for F.R.C.S. and offer exceptional opportunities for general experience with a Senior Surgical Registrar in a busy acute unit of 70 Beds.

Applications, with copies of recent testimonials, to Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTHAMPTON CHILDREN'S HOSPITAL. (Recognised by Conjoint Board for D.C.H.) HOUSE OFFICER required. Total establishment of 3 residents. Salary, &c., as nationally advocated.

Applications, with copies of testimonials, to be submitted by 22nd March, 1958, to the Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTHAMPTON. ROYAL SOUTH HANTS HOSPITAL. (274 Beds. Recognised for F.R.C.S.) ORTHOPÆDIC HOUSE SURGEON (post recognised for pre-registration). The Hospital is the centre to which all trauma from a large industrial town and port is directed, thus providing excellent experience in the treatment of traumatic conditions; patients with orthopædic conditions are drawn from a wide area.

Applications, with copies of testimonials, should be sent as soon as possible to the Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SIDCUP, KENT. QUEEN MARY'S HOSPITAL. Senior HOUSE OFFICER (gynæcology and general surgery) required immediately. The duration of the post is for 1 year in the first instance.

Applications, stating age, qualifications and experience, together with names and addresses of 2 referees, should be sent to the Secretary.

SLOUGH, BUCKINGHAMSHIRE. UPTON HOSPITAL. Locum MEDICAL REGISTRAR required 31st March–13th April.

Applications, with names of 2 referees, to Secretary.

SLOUGH, BUCKINGHAMSHIRE. UPTON HOSPITAL. HOUSE OFFICER required in Department of Obstetrics and Gynæcology to work with part-time Registrar. Post vacant 8th April. Not recognised for D.Obst.R.C.O.G.

Applications, with names of 2 referees, to Secretary by 25th March.

ST. ALBANS CITY HOSPITAL, St. Albans, Hertfordshire. HOUSE PHYSICIAN (House Officer grade) required for duties mainly in the Pædiatric Department. Post vacant approximately 20th April, 1958, and tenable for 6 months. Preference given to candidates seeking pre-registration posts under the Medical Act, 1950.

Applications to Secretary, Mid Herts Group Hospital Management Committee, Bleak House, Catherine-street, St. Albans.

ST. ALBANS CITY HOSPITAL, St. Albans, Hertfordshire. (384 Beds.) HOUSE PHYSICIAN (House Officer grade) required for 1 of the 2 medical firms for duties mainly on the acute wards. Post vacant 3rd April, 1958, and tenable for 6 months. Preference given to candidates seeking post under the Medical Act, 1950.

Applications to Secretary, Mid-Hertfordshire Group Hospital Management Committee, Bleak House, Catherine-street, St. Albans.

ST. ALBANS CITY HOSPITAL, St. Albans, Hertfordshire. (384 Beds.) HOUSE SURGEON (House Officer grade) required for 1 of the 2 surgical teams. Post recognised for F.R.C.S. Post vacant 16th April, 1958, and tenable for 6 months. Preference given to candidates seeking post under the Medical Act, 1950.

Applications to Secretary, Mid-Hertfordshire Group Hospital Management Committee, Bleak House, Catherine-street, St. Albans.

STIRLING AND CLACKMANNAN HOSPITALS BOARD OF MANAGEMENT. There is a vacancy for a Locum SENIOR HOUSE OFFICER in General Surgery at Clackmannan County Hospital commencing on 1st April, 1958, for approximately 3 months.

Applications, giving 2 names for reference, should be sent immediately to the Group Medical Superintendent, Stirling Royal Infirmary.

STOCKPORT INFIRMARY. (163 Beds.) Applications are invited for the post of HOUSE OFFICER (general surgery), vacant 7th April, 1958. This is an approved pre-registration post and is recognised for the F.R.C.S.

Applications, with copies of 2 testimonials, to the Group Secretary, Stockport and Buxton Hospital Management Committee, 59B, Shaw-heath, Stockport.

STOKE-ON-TRENT. CITY GENERAL HOSPITAL. SENIOR HOUSE OFFICER (general surgery) required. Hospital recognised for F.R.C.S. Post vacant very shortly.

Applications to Hospital Secretary as soon as possible.

STOKE-ON-TRENT. NORTH STAFFORDSHIRE ROYAL INFIRMARY. SENIOR HOUSE OFFICER (E.N.T.) required. Recognised F.R.C.S. and D.L.O.

Detailed applications with copy testimonials to Hospital Secretary, Royal Infirmary, Stoke-on-Trent.

SWANSEA HOSPITAL, SWANSEA. (413 Beds.) Glantawe HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the resident post of SENIOR HOUSE OFFICER in the Traumatic and Orthopædic Department of the above Hospital. The post is recognised under the F.R.C.S. regulations for 6 months' casualty training. It offers exceptional experience in all aspects of traumatic surgery as occurring in a large industrial centre and port.

Applications, stating age and experience together with copies of 2 recent testimonials, should be forwarded to the Hospital Secretary. T. E. JONES, Group Secretary.

SWINDON AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Swindon Hospitals. Applications invited for post of RESIDENT HOUSE PHYSICIAN in Acute Medical Unit of 64 Beds at St. Margaret's Hospital. Recognised for training under pre-registration internship regulations.

Full details, with names of 3 referees, to Secretary, 7, Okus-road, Swindon, immediately.

TAUNTON AND SOMERSET HOSPITAL. Applications are invited for HOUSE OFFICER (E.N.T.). Post vacant now. Post-registration appointment, recognised for F.R.C.S. and D.L.O.

Applications, stating age, nationality and qualifications, together with the names of 2 referees, should be forwarded to the Group Secretary, Taunton Hospital Management Committee, c/o Musgrove Park Hospital, Taunton, Somerset.

TAUNTON AND SOMERSET HOSPITAL. Applications are invited for HOUSE OFFICER (general medicine). Post vacant 11th April, 1958. Recognised for pre-registration candidates.

Applications, stating age, nationality, and qualifications, together with the names of 2 referees, should be forwarded to the Group Secretary, Taunton Hospital Management Committee, c/o Musgrove Park Hospital, Taunton, Somerset.

TAUNTON AND SOMERSET HOSPITAL. Applications are invited for the post of SENIOR HOUSE OFFICER (obstetrics and gynæcology). Vacant 11th May, 1958. The Department consists of the Area Maternity Unit of 50 Beds (recently modernised and extended) and a gynæcological ward of 25 Beds. Recognised for the M.R.C.O.G.

Applications, stating age, qualifications, nationality, and experience, together with the names of 2 referees, should be forwarded immediately to the Group Secretary, Taunton Hospital Management Committee, c/o Musgrove Park Hospital, Taunton, Somerset.

TAPLOW, near MAIDENHEAD. CANADIAN RED CROSS MEMORIAL HOSPITAL. SENIOR HOUSE OFFICER to Department of Pathology required for post vacant 1st April. Post offers scope for participation in routine work of all sections of department and in research undertaken by Special Unit for Juvenile Rheumatism.

Applications, stating age, qualifications and experience, with copies of 2 recent testimonials, to Secretary.

TORQUAY. TORBAY HOSPITAL. Senior Resident HOUSE OFFICER (medicine) required end April, 1958. There is a complement of 6 Resident House Officers.

Applications, stating qualifications, age, nationality, with copy testimonials (quoting reference F.955/90) to the Group Secretary, Torquay District Hospital Management Committee, Torbay Hospital, Torquay, S. Devon.

TUNBRIDGE WELLS (near). PEMBURY HOSPITAL, PEMBURY. Applications invited for appointment of SENIOR ORTHOPÆDIC HOUSE SURGEON AND CASUALTY OFFICER (Senior House Officer grade) to begin duties as soon as possible. Recognised F.R.C.S. (Eng.) and tenable for 1 year. Work includes treatment of long- and short-stay cases and traumatic surgery with large Outpatient and Fracture Clinics under 2 Consultants.

Apply, stating age, qualifications and experience, together with 3 testimonials, to Group Secretary, Sherwood Park, Pembury-road, Tunbridge Wells.

WARWICK (near). CENTRAL MENTAL HOSPITAL. (1400 Beds.) SENIOR HOUSE OFFICER, Neurosis Unit, Adult and Child Psychiatry Clinics, Departments of Electroencephalography, Occupational Therapy, Psychology and Social Work. Recognised for D.P.M. Accommodation available. Post vacant.

Applications, with names and addresses of 3 referees, to Medical Superintendent.

WATFORD, HERTFORDSHIRE. PEACE MEMORIAL HOSPITAL. (211 Beds.) ORTHOPÆDIC HOUSE SURGEON (with certain casualty duties) required. Post recognised for F.R.C.S. (Eng.) examination. The orthopædic service is in the charge of a Consultant and Registrar closely associated with a postgraduate teaching hospital.

Applications, with copies of 2 testimonials, to the Administrator.

WATFORD, HERTFORDSHIRE. PEACE MEMORIAL HOSPITAL. (211 Beds.) Applications are invited for the post of RESIDENT ANÆSTHETIST (Senior House Officer grade) to the Watford Hospitals.

Applications, together with copies of not more than 2 recent testimonials, to the Administrator.

WATFORD, HERTFORDSHIRE. PEACE MEMORIAL HOSPITAL. (211 Beds.) Applications are invited for the post of HOUSE SURGEON at the above Hospital. This is a pre-registration post and is recognised for F.R.C.S. Salary according to the National Health Service scale.

Applications, with copies of recent testimonials, to the Administrator.

WATFORD. SHRODELLS HOSPITAL. Applications are invited for the post of HOUSE OFFICER (Senior House Officer grade) to the Pædiatric Unit of 38 Beds. Post recognised for the D.C.H. To take up duty at the beginning of April.

Applications, together with copies of 2 recent testimonials, should reach the Medical Administrator as soon as possible.

WESTON-SUPER-MARE GENERAL HOSPITAL. (104 Beds.) Applications are invited from duly qualified medical practitioners for the pre-registration appointment (resident) of HOUSE SURGEON. Immediate vacancy.

Applications, stating age, qualifications, together with names and addresses of 2 referees, should be addressed to the Secretary, Weston-super-Mare Hospital Management Committee.

WEYMOUTH AND DISTRICT HOSPITAL. (124 Beds.) HOUSE SURGEON (Male or Female) required for resident pre-registration post vacant 1st April, 1958, and tenable for 6 months. Recognised for F.R.C.S. examination.

Applications, stating age, qualifications, together with copy testimonials, to Group Secretary, West Dorset Hospital Management Committee, Damers-road, Dorchester, Dorset, immediately.

WEYMOUTH AND DISTRICT HOSPITAL. (124 Beds.) CASUALTY OFFICER (Senior House Officer grade) required for approximately 5 months.

Applications, stating age, qualifications, nationality and experience, together with copy testimonials, to Group Secretary, West Dorset Hospital Management Committee, Damers-road, Dorchester, Dorset, immediately.

WINCHESTER. ROYAL HAMPSHIRE COUNTY HOSPITAL. (327 Beds.) HOUSE PHYSICIAN (post-registration) to the Pædiatric Department. Vacant 28th March. Preference will be given to applicants wishing to specialise in pædiatrics. The Department is recognised for the D.C.H.

Applications, with copies of 2 testimonials, to the Group Secretary.

WINCHESTER. ROYAL HAMPSHIRE COUNTY HOSPITAL. (327 Beds.) HOUSE SURGEON (post recognised by Royal College of Surgeons) required for general surgery with some E.N.T. duties. Approved pre-registration post. Vacant immediately.

Applications, with copies of 2 testimonials, to Group Secretary.

WIGAN. ROYAL ALBERT EDWARD INFIRMARY. (200 Beds.) SENIOR HOUSE OFFICER in Orthopædic Surgery.

Applications to Secretary, Royal Albert Edward Infirmary, Wigan.

WINDSOR. KING EDWARD VII HOSPITAL. Obstetric AND GYNÆCOLOGICAL HOUSE SURGEON required, Male or Female, for post vacant 22nd April. Post recognised for both M.R.C.O.G. and D.Obst.R.C.O.G. Not a pre-registration post. Successful candidate will be resident at Old Windsor Unit of Hospital.

Applications, with copies of recent testimonials, or names of 3 referees, stating age, nationality, qualifications, with dates, to Secretary.

WINDSOR. KING EDWARD VII HOSPITAL. Registrar (Casualty Officer), resident, required immediately. There is an Accident Unit of 30 beds at the Hospital and with the Casualty Department forms part of the Accident Service for the Windsor Group and includes duties with the E.N.T. and Eye Departments. Candidates should have had previous experience in the treatment of acute injuries.

Application forms from and returnable to Secretary, Windsor Group Hospital Management Committee, Alma-road, Windsor.

WOLVERHAMPTON GROUP OF HOSPITALS. Whole-time SENIOR REGISTRAR in E.N.T. Surgery. Duties mainly at the Royal Hospital, Wolverhampton (an associated hospital of the Birmingham University Medical School). Higher qualification required. Resident or non-resident. The successful candidate many subsequently be required to spend not more than 2 years in a selected hospital of the United Birmingham Hospitals in accordance with the arrangements for the interchange of Registrars agreed between the two Boards.

Application forms from the Secretary, Birmingham Regional Hospital Board, 10, Augustus-road, Birmingham 15, to be returned by 31st March, 1958.

WOLVERHAMPTON. THE ROYAL HOSPITAL. (An Associated Hospital of the Birmingham University Medical School.) E.N.T. HOUSE OFFICER (Senior House Officer grade). Post recognised for the D.L.O. and F.R.C.S. examinations. Vacant immediately.

Apply, with copies of 2 testimonials, to the Secretary.

WOLVERHAMPTON. THE ROYAL HOSPITAL. (An Associated Hospital of the Birmingham University Medical School.) ORTHOPÆDIC HOUSE SURGEON for Fracture and Orthopædic Department. Post recognised for F.R.C.S. Vacant immediately.

Apply, with 2 testimonials, to the Secretary.

WORCESTER ROYAL INFIRMARY. (213 Beds.) House PHYSICIAN (pædiatrics) required immediately. Busy department comprising very modern unit of 26 Beds. Post recognised for D.C.H.

Applications to Hospital Secretary.

WORCESTER ROYAL INFIRMARY. House Surgeon (pre-registration or otherwise) required immediately for Orthopædic Department of this busy general Hospital of 213 Beds. The appointment offers wide and varied experience.

Applications to Hospital Secretary.

ST. JOHN'S, NEWFOUNDLAND, CANADA. GENERAL HOSPITAL. (475 Beds.) The above Hospital has vacancies for INTERNES, beginning July, 1958, for which applications are invited; salary $2500 p.a. less $528 for maintenance. There is a full teaching programme; the Hospital is fully approved by the Canadian Medical Association for Interne training, approved by the Royal College of Physicians and Surgeons in Canada for postgraduate training towards certification and also recognised under the United Kingdom Medical Act for pre-registration year. Transport to St. John's will be paid and on completion of 1 year's service, return fare to the United Kingdom will be provided.

Applications, with full details as to age, &c., together with names of 2 referees, should be forwarded immediately to: Dr. E. WILSON, Superintendent.

QUEENSLAND RADIUM INSTITUTE. A vacancy exists for the position of RESIDENT MEDICAL OFFICER in the Queensland Radium Institute. Applicants should have completed 1 or 2 years of postgraduate experience when duties begin. Commencing salary for appointee with 1 year's experience £A1379½, 2 years' experience £A1939½, subject to future basic wage adjustments. Board and lodging provided or £100 living-out allowance in lieu thereof. Appointee will have opportunity for specialist training in radiotherapy in a progressive centre equipped with therapeutic apparatus ranging up to a supervoltage unit. Further particulars obtainable from the Director, Queensland Radium Institute, Herston-road, Brisbane. The Chairman of the Institute (Dr. A. Fryberg) will be in England about mid-April and may be interviewed by arrangement at Queensland House, 409–410, The Strand, London, W.C.2.

Applications, enclosing testimonials, should be addressed to the Manager, Brisbane and South Coast Hospitals Board, Herston-road, Brisbane, Queensland, Australia, before 30th April, 1958.

U.S.A. UNIVERSITY OF MINNESOTA MEDICAL CENTER. ANESTHESIOLOGY RESIDENCIES at the above Center. 2 or 3-year programme with clinical and didactic instruction in all phases of anæsthesia. Board approval. Positions starting every month.

Address, F. H. VANBERGEN, M.D., University of Minnesota Medical Center, Minneapolis 14, Minnesota.

U.S.A. BRIDGEPORT HOSPITAL, Bridgeport, Connecticut. Approved ROTATING INTERNSHIPS and RESIDENCIES available in a general hospital of 387 Beds and 60 Bassinets. Stipend of $190 per month in addition to full maintenance and uniforms. Exchange Visitor Program participant.

Address inquiries to: Chairman, Committee on Medical Education, Bridgeport Hospital, Bridgeport 10, Connecticut, U.S.A.

U.S.A. NORTON MEMORIAL INFIRMARY, Louisville, KENTUCKY, U.S.A. A 290-Bed general hospital, approved by the American Medical Association for ROTATING INTERNSHIPS of 1-year duration. Approved under Exchange Visitor Program. Only graduates from approved medical schools considered. Rotating services in medicine, surgery, obstetrics and pædiatrics. Stipend $200 per month, and full maintenance for bachelors.

Apply airmail to Administrator.

SOUTH AUSTRALIA. ADELAIDE CHILDREN'S HOSPITAL, INC. Applications are invited from Medical Graduates for appointment as ASSISTANT PATHOLOGIST in the Department of Morbid Anatomy at the above Hospital.

Duties: to assist with the routine work of the Department, to undertake research, and to help with postgraduate and undergraduate teaching. Opportunities will be available for the successful applicant to work for a higher degree.

Qualifications: must be a Medical Graduate. Some experience in the other branches of clinical pathology are desirable, but not essential.

All applicants are requested to submit full professional and personal details, and name at least 3 referees. The salary payable will be within the range of £1873–£2328 p.a., and will be paid according to experience and qualifications. Normal leave benefits will be available, and also superannuation benefits. The term of appointment is for a period of 3 years with eligibility for reappointment.

All applications must be addressed to—

E. H. D. LINES, Manager and Secretary.
Adelaide Children's Hospital, Inc.,
72, King William-road,
North Adelaide, South Australia.

UGANDA MEDICAL DEPARTMENT. Hospital appointments. Applications are invited for:—

(*a*) Male RESIDENT MEDICAL OFFICERS (Interns) at Mulago Hospital, Kampala, Uganda, for normal internship duties in the departments of medicine, surgery, and obstetrics. Appointments on agreement for a period of 12 months with salary rate £618 a year for first 6 months and £645 a year for second 6 months, and a messing allowance of £144 a year. Free furnished quarters, including linen, cutlery, china and glass, together with light, fuel, and water provided. Married quarters not provided, married candidates may not be accompanied by their wives. Free air passage provided on appointment and on satisfactory completion of agreement. Selected candidates may apply for appointments to the Medical Branch of Her Majesty's Overseas Civil Service on the expiration of internships. Candidates should verify from their licensing bodies that the posts at the Mulago Hospital are approved by them for pre-registration training under the Medical Act, 1950.

(*b*) RESIDENT MEDICAL OFFICER (for doctor already on the British Medical Register) at the European and Asian Hospital, Kampala, to work under the direction of a specialist surgeon, physician or obstetrician. The general administration of the Hospital (which has 92 Beds) is under a Medical Superintendent. Appointment will be on contract for 1 year with gratuity (taxable) of 13½% salary and then selected officers may be offered appointment to permanent and pensionable post on 2 years' probation. Candidates from National Health Service may retain superannuation rights and receive gratuity (taxable) of 20% of salary after engagement.

Salary scale ranges from £1284 to £2115 a year. Starting salary determined according to qualifications and experience. Free passages (up to 4 tourist class air fares) provided in both directions for officer, wife, and dependent children. Quarters are provided at rental between £21 and £78 a year; items of hard furniture supplied at rental of £12–£24 a year. Income-tax at local rates.

Application forms from Director of Recruitment, Colonial Office, London, S.W.1 (quoting reference BCD.117/9/016).

Public Appointments

FACTORY DOCTORS. Factories Acts 1937 and 1948. The following appointments as Appointed Factory Doctor are vacant. Apply to Chief Inspector of Factories, 19, St. James's-square, London, S.W.1.

District	*County*	*Latest date for receipt of applications*
SHIFNAL ..	.. SALOP	.. 5TH APRIL, 1958
HIRWAUN	.. GLAMORGAN ..	.. 5TH APRIL, 1958

MINISTRY OF SUPPLY, Chemical Defence Experimental Establishment, PORTON, SALISBURY, WILTSHIRE. 2 PHYSIOLOGISTS (Male) required: (1) Principal Scientific Officer (minimum age 31) with medical qualification and first or second class honours degree in physiology, research experience in problems of applied and human physiology required. (2) Senior Scientific Officer with first or second class honours degree in physiology and at least 3 years' research experience, preferably in application of physical methods to biological problems. Experience in respiratory physiology or hæmodynamics an advantage. Salary: Principal Scientific Officer £1370–£1950; Senior Scientific Officer £1130–£1330 (superannuable).

Forms from Ministry of Labour and National Service, Technical and Scientific Register (K), 26, King-street, London, S.W.1, quoting G87/8A. Closing date 5th April, 1958.

DERBYSHIRE COUNTY COUNCIL. County Health DEPARTMENT. MATERNAL AND CHILD WELFARE MEDICAL OFFICER (Female). Applications are invited from fully qualified medical practitioners for this whole-time superannuable post. Candidates should be experienced in antenatal work, midwifery, and children's diseases, as they will be required to hold consultations at the Council's Maternity and Child Welfare Clinics and Centres, and to perform such other duties as may be required. Salary £1050–£50–£1200–£55–£1475 p.a., plus a car allowance.

Particulars and application forms are obtainable from Dr. J. B. S. MORGAN, County Medical Officer, St. Mary's Gate, Derby, and should be returned to him duly completed not later than 24th March, 1958.

DERBYSHIRE COUNTY COUNCIL. Mental Health DEPARTMENT. ASSISTANT MEDICAL OFFICER FOR MENTAL HEALTH. Applications invited from registered medical practitioners with D.P.H. and/or D.P.M. Recognition by Ministry of Education for ascertainment of subnormal children, and experience in mental health generally and ascertainment of handicapped essential. Salary: £1210–£55(5)–£50(4)–£1685 p.a. Car and subsistence allowances. Post superannuable.

Particulars and application forms obtainable from County Medical Officer, County Offices, St. Mary's Gate, Derby, closing date 24th March, 1958. Canvassing disqualifies.

BIRMINGHAM. CITY OF BIRMINGHAM PUBLIC HEALTH DEPARTMENT. Applications are invited from registered medical practitioners for post of ADMINISTRATIVE MEDICAL OFFICER OF HEALTH (Male or Female). Candidates should hold the Diploma of Public Health. This is a Sectional Post and the Medical Officer will be responsible to the Medical Officer of Health for the administration of activities relating to Maternity and Child Welfare Services and will also be available for all other work of the Health Department, such as housing, epidemiology and infectious diseases, &c. Applicants should, therefore, have had extensive experience in all branches of public health work. Salary scale £2065–£75–£100 (2)–£2340 p.a. Commencing salary within the scale will depend upon the medical officer's experience. Pension scheme (including Widows and Orphans); medical examination. The officer appointed will be required to devote his/her whole time to official duties and the appointment will be subject to 3 months' notice on either side.

Applications, with names of 3 persons to whom reference may be made, to be sent to the Medical Officer of Health, Council House, Birmingham, 3, not later than 26th March, 1958.

WARWICKSHIRE COUNTY COUNCIL. County Medical OFFICER OF HEALTH'S DEPARTMENT. Applications are invited from registered medical practitioners for the appointment of ASSISTANT COUNTY MEDICAL OFFICER OF HEALTH, which is in the north-eastern area of the County. Preference will be given to those holding the D.P.H. or D.C.H. and with previous experience. Conditions of service and salary (£1050–£1475) will be in accordance with the Whitley Council. The successful candidate will be required to provide a motor car in the performance of duties, for which Whitley Council scale allowances are payable. Grant towards removal expenses will be considered.

Further particulars, including details of duties, and application forms may be obtained from the County Medical Officer of Health, Shire Hall, Warwick. Closing date for applications is 29th March, 1958. L. EDGAR STEPHENS, Clerk of the Council.

Shire Hall, Warwick. 18th February, 1958.

FEDERAL ARMY OF RHODESIA AND NYASALAND. Vacancies: Medical Officers. Applications are invited for appointment as Full-time MEDICAL OFFICERS in the Rhodesia and Nyasaland Medical Corps. Successful applicants (preferably single with Service experience, age-limit 40 years) will be required to attest in and serve as regular officers in the Corps. Appointments are in the rank of Captain on scale £1371 p.a., plus 6 annual increments to £1621 p.a. In addition to the foregoing, a professional allowance of £200 p.a. will be paid.

Applications should be addressed to the Federal Military Liaison Officer, Rhodesia House, 429, Strand, London, W.C.2, who will arrange an appointment to discuss the career offered.

GOVERNMENT OF THE FEDERATION OF NIGERIA. MEDICAL OFFICER OF HEALTH required for administration of Public Health and control of sanitary matters, or if posted to sea or airport, the duties of Port Health Officer. May be required to perform general duties of Medical and Health Officer and other duties in connection with epidemic diseases. Must possess medical qualifications registrable in the United Kingdom, and D.P.H. Appointment:—

(*a*) on short-term contract with inclusive salary from £1536 to £2286 p.a. On completion of contract gratuity (taxable) is paid of £37 10s. for each completed period of 3 months' service (including leave).

(*b*) from National Health Service with inclusive salary from £1326 to £1950 p.a., candidate retaining superannuation rights and receiving gratuity (taxable) of 20% of aggregate of salary.

Quarters at low rental. Free return passages for officer and wife. Return passages for children, to age 18, provided cost does not exceed that of 2 adult return passages in any 1 tour of service. Children's (separate domicile) allowance of £75 a year for each child under 18, ceasing if children join parents in Nigeria. Income-tax at local rates. Local leave permissible and generous home leave after each tour.

Application forms from Director of Recruitment, Colonial Office, London, S.W.1 (quoting BCD.117/14/07).

Hospital Services: Non-Medical Appointments

CARDIFF. UNITED CARDIFF HOSPITALS. Applications are invited for the post of HOSPITAL BIOCHEMIST (Senior grade) in the Department of Clinical Pathology at Llandough Hospital, Penarth, Glamorgan. This is 1 of the 2 main teaching hospitals of the United Cardiff Hospitals. Whitley Council salary £1100–£1500 p.a. and conditions of service.

Applications, with full details and names of 2 referees, to be addressed to the Secretary, United Cardiff Hospitals, Cardiff Royal Infirmary, Newport-road, Cardiff.

OXFORD. UNITED OXFORD HOSPITALS. Department OF CLINICAL BIOCHEMISTRY, RADCLIFFE INFIRMARY, OXFORD. Applications are invited for the post of HOSPITAL BIOCHEMIST (senior grade) in the routine biochemical section of this department. Candidates must hold a university degree in science or an equivalent qualification. Salary and conditions of service in accordance with the Whitley scale. Details of the post may be obtained from the Director of the Biochemistry Department.

Applications, with the names and addresses of 2 referees, should be sent to the Administrator, Radcliffe Infirmary, Oxford, not later than 2 weeks after the appearance of this advertisement.

General Practice

For an ***Executive Council post*** *(England and Wales) apply on form* **E.C.16A** *obtainable from the council. Mark envelope "Vacancy."*

WILLESDEN. Applications invited for Vacancy occasioned by death of Female practitioner. List at present approximately 2600. "Designated" area. Premises may be available. Apply on Form E.C.16A before 22nd March, 1958, to: The Clerk, Middlesex Executive Council. North West House, 119/127, Marylebone-road, London, N.W.1.

LOWESTOFT, SUFFOLK. Applications invited for mainly urban VACANCY, due to death. List at present approximately 3285. "Intermediate" area. Surgery premises probably available for purchase. Apply on Form E.C.16A by 26th March to undersigned, from whom further details may be obtained.

32, Silent-street, Ipswich. A. P. LUCAS, Clerk, East Suffolk County Executive Council.

URBAN DISTRICT OF COULSDON AND PURLEY (Old Coulsdon). Applications invited for VACANCY which will arise on 5th July, 1958, in above Urban District (intermediate) List at present about 1750. Retiring doctor's residence and surgery not available. Applications on forms E.C.16A to reach the undersigned not later than 27th March, 1958.

Surrey Executive Council, 187, Ewell-road, Surbiton, Surrey. S. H. BENNETT, Clerk of the Council.

Miscellaneous

David Brown Industries Limited require the services of a Senior Medical Officer to be responsible for the industrial medical services of the Company. The post is based on Huddersfield and additional part-time medical assistance is provided at certain branches. Candidates for the post should be not less than 35 years or more than 45 years of age. Previous experience in industry is essential and D.I.H. would be considered an advantage. Salary will be in accordance with the B.M.A. scale. The post is pensionable.

Replies, giving full details of qualifications, experience, &c., should be addressed to the Deputy Managing Director, DAVID BROWN INDUSTRIES LIMITED, Durker Roods, Meltham, near Huddersfield, Yorkshire.

MSL have been retained to advise on the appointment of a

DIRECTOR OF RESEARCH

This is a new scientific appointment offering considerable freedom in creating and directing a research organisation. It will interest those already in charge of academic or industrial research programmes.

The person appointed will be responsible for planning and equipping laboratories near London, drawing up a long-term research programme and selecting his own research team. He will be encouraged to continue his scientific affiliations both at home and abroad.

In addition to creative satisfaction, the post offers tangible rewards of interest to those already earning £4000 or more.

This new research establishment will be largely autonomous and will be complementary to the extensive research interest of the parent company, which is one of the larger ethical pharmaceutical firms in the U.S.A.

Candidates must have organised and conducted research in fields relating to biochemistry, physiology, pharmacology or experimental therapeutics and should preferably hold a higher scientific or medical qualification. Previous experience in the pharmaceutical industry is by no means essential.

Please send details of qualifications, experience and publications to R. A. Denerley at the address below, quoting reference AN.793. No information will be disclosed to our client until candidates have been told the company's identity and have given permission after confidential discussion.

MANAGEMENT SELECTION LIMITED
17, Stratton-street, London, W.1

Locum required for rural group practice. Car essential. Usual terms. 28th March–15th April, 10th May–1st June, 14th June–30th June, and 26th July–13th September.—Apply Dr. W. J. H. LORD, The Surgery, Alford, Lincs.

Doctors requiring applications, theses copied: Write to MANTON (WESTMINSTER) LTD., 98, Victoria-street, S.W.1 (VIC. 0141), who are specialists.

"Pregnancy Diagnosis by the Xenopus Method," 24-hour service. Send specimens of urine and £2 2s. fee. Hæmatology, Biochemistry, Flame Photometry.—WELBECK BIOLOGICAL LABORATORIES, 26, Park-crescent, Portland-place, W.1 (MUSeum 5386–7).

Microscopes. Highest prices paid for good modern types. Send or bring your equipment for valuation.—WALLACE HEATON LTD., 127, New Bond-street, W.1.

Medical Secretary, full-time, required by consulting physician, Harley Street.—Address No. 380, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Polygraphs. A department of Physiology would be glad to receive unwanted polygraphs for pulse recording.—Address No. 381, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

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Inability to take aspirin . . .

IT HAS BEEN reported (*Brit. med. J.*, 1: 444, 1957) that of 178 rheumatic patients, 25% could not take plain aspirin in adequate dosage.

Of this 25%, however, the great majority tolerated a modified aspirin such as Paynocil.

Not only are Paynocil tablets usually well tolerated by the stomach (even on the heavy dosage needed for rheumatoid arthritis), but they are extremely palatable, disintegrate instantly on the tongue without water, and cause no discomfort or unpleasant after-sensation.

. . . indicates PAYNOCIL

non-irritant, palatable, quick-dispersing aspirin

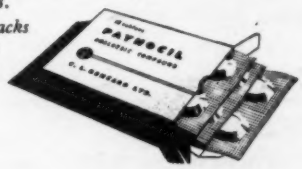
FOR ADULTS

PAYNOCIL

EACH TABLET CONTAINS

Acetylsalicylic acid ..... 10 grains
Aminoacetic acid..... 5 grains

PACKAGES in sealed foil strips:
Cartons of 18.
Dispensing packs of 240: basic N.H.S. cost (tax free) 21/8d.



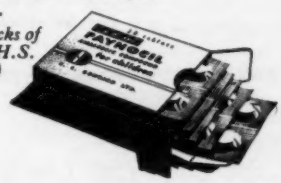
FOR CHILDREN

Junior PAYNOCIL

EACH TABLET CONTAINS

Acetylsalicylic acid ..... 2½ grains
Aminoacetic acid ..... 1¼ grains

PACKAGES in sealed foil strips:
Cartons of 20.
Dispensing packs of 240: basic N.H.S. cost (tax free) 12/-.



Detailed recommendations for dosage in rheumatoid arthritis will be gladly supplied on request

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THE BASIC TREATMENT. PARTICULARLY EFFECTIVE IN MILD OR MODERATE CASES

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FOR THOSE CASES SHOWING INADEQUATE RESPONSE TO SERPASIL ALONE

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INDICATED WHERE DROWSINESS OCCURS DURING RAUWOLFIA THERAPY

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